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VOLUME XXVIII NUMBER 2

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of the

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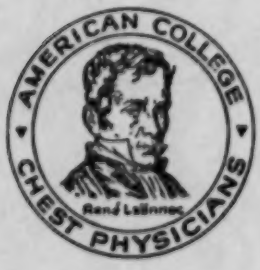

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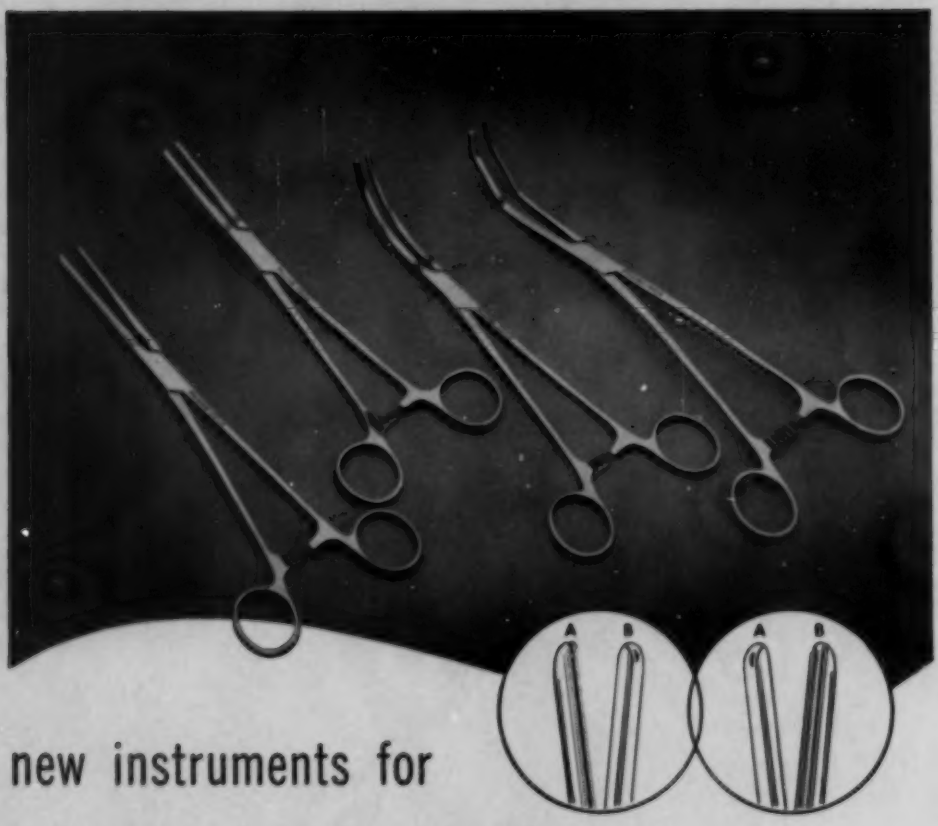

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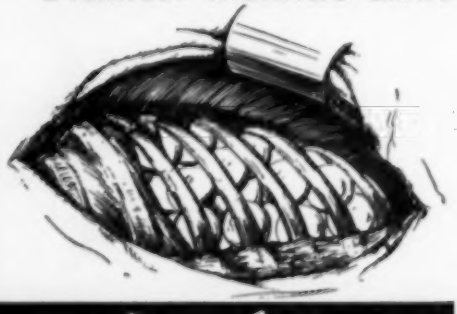

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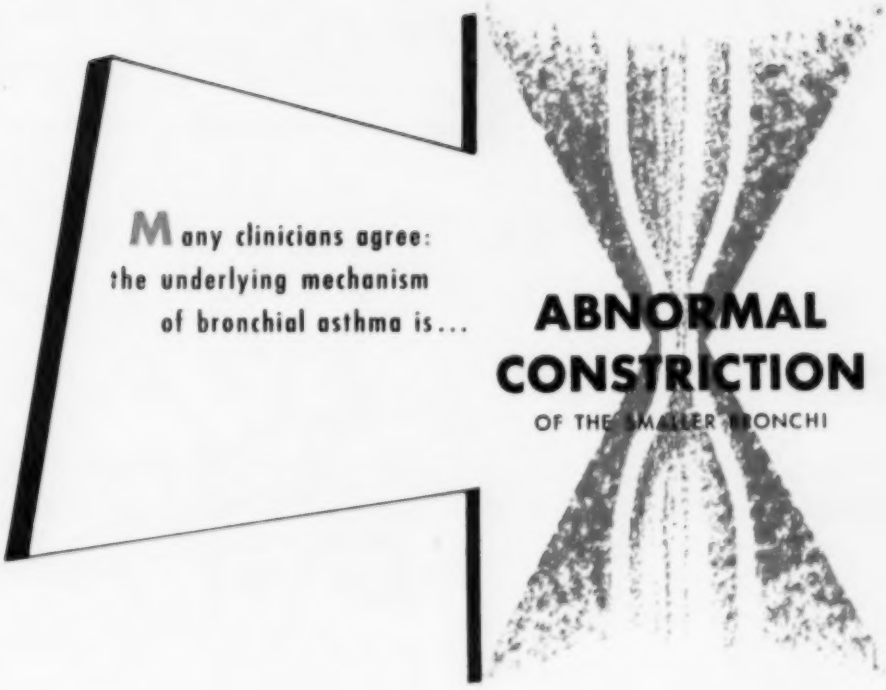

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3. Segal, M. S.: Facts and Fancies in the Management of the Seriously Ill Patient with Bronchial Asthma. Dis. of Chest, 14:795, 1948.

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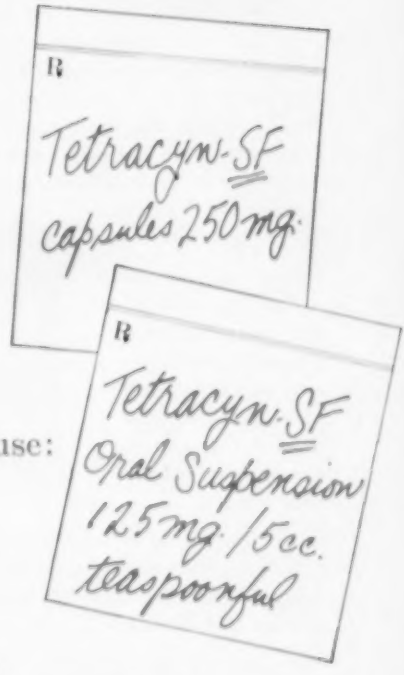

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1. Pollack, H., and Halpern, S. L.: Therapeutic Nutrition, Prepared in Collaboration with the Committee on Therapeutic Nutrition, Food and Nutrition Board, National Research Council, Washington, D. C., 1952. 2. Marti-Ibáñez, F.: Antibiotic Med. *1*:247 (May) 1955. 3. Dumas, K. J.; Carlozzi, M., and Wright, W. A.: Antibiotic Med. *1*:296 (May) 1955. 4. Milberg, M. B., and Michael, M., Jr.: Ann. New York Acad. Sc., In press. 5. Prigot, A.: Ibid.

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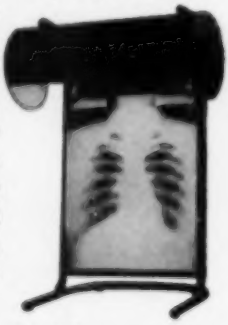

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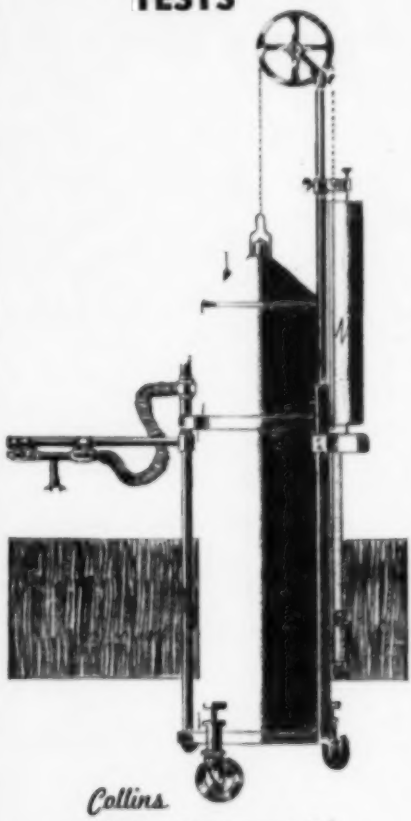

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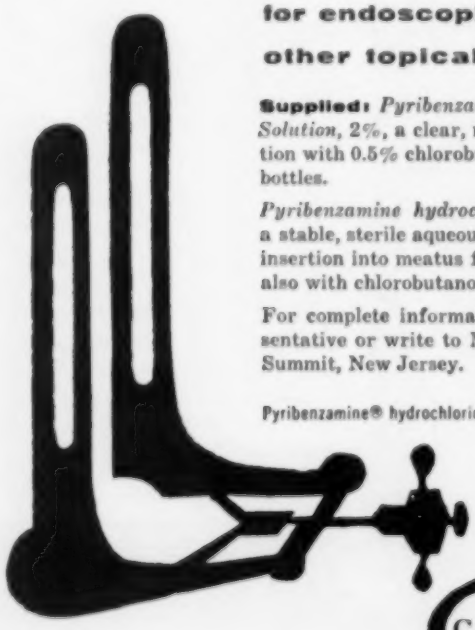

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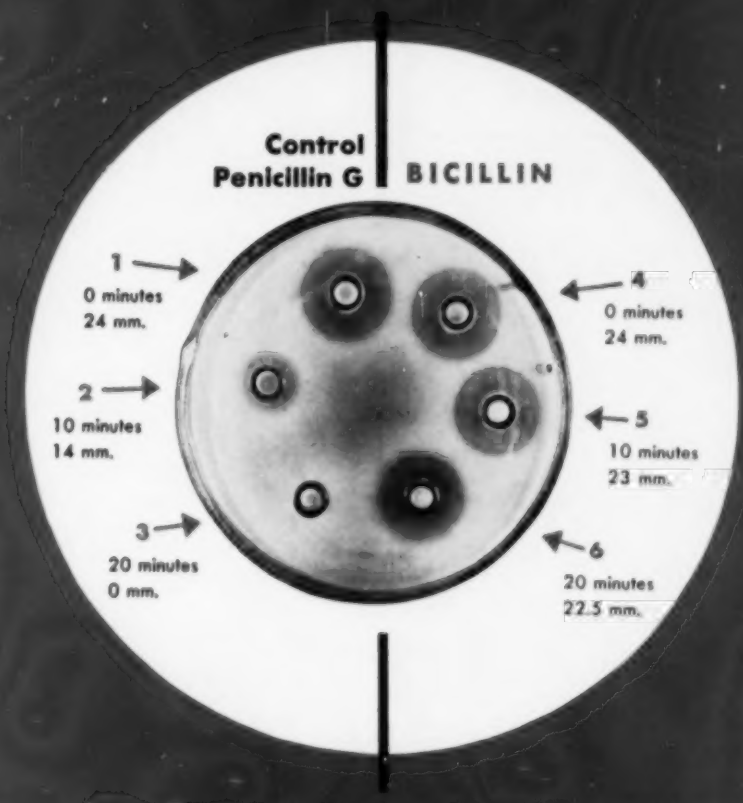

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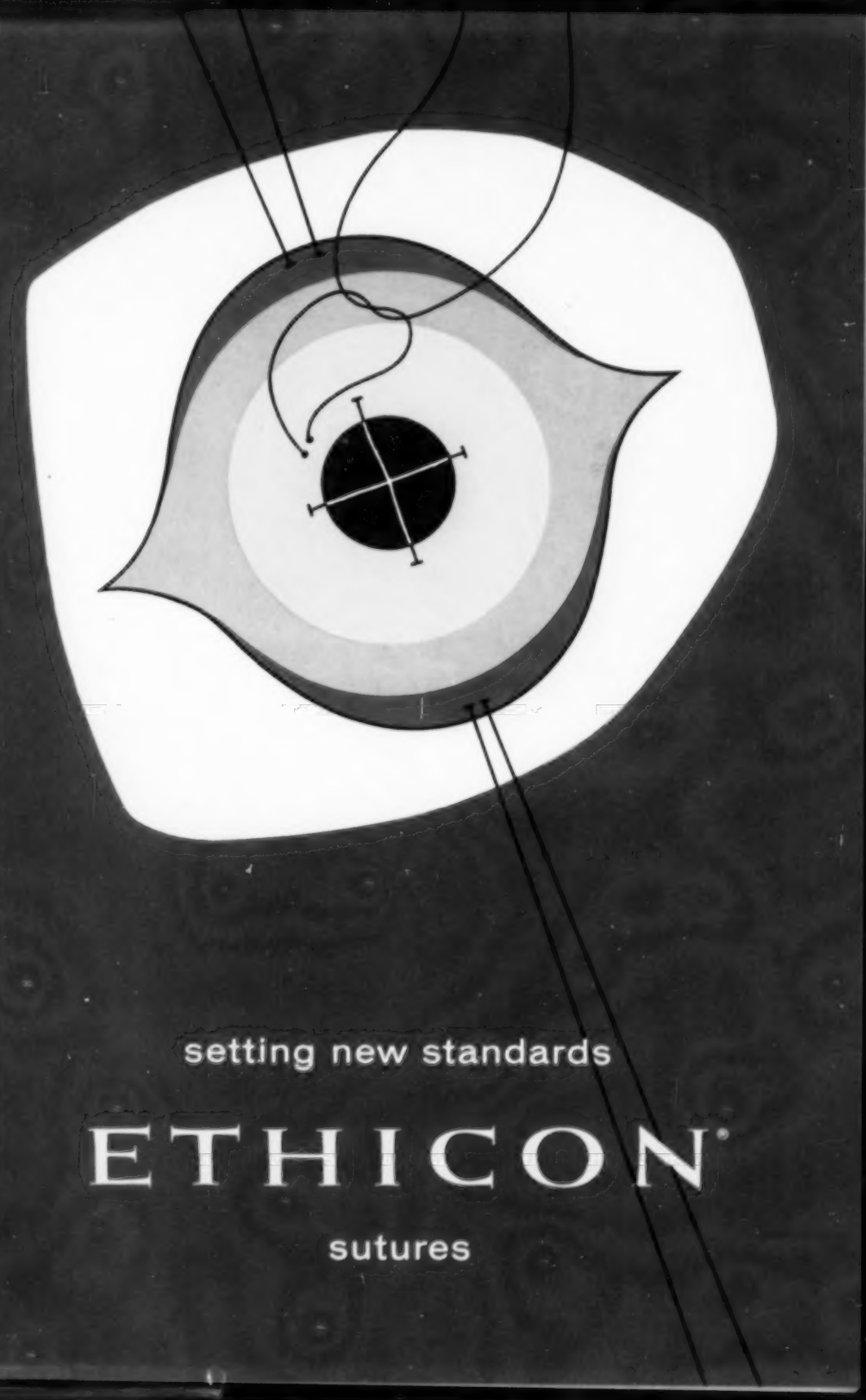
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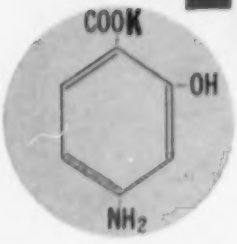

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2. *Cohen, R. V., Molthan, L., and Zarafonetis, C. J. D.: Clinical Studies of Various Forms of PAS (with special reference to plasma concentrations). Read before the American Trudeau Society, Annual Meeting, Milwaukee, Wisconsin, May 23-27, 1955.*

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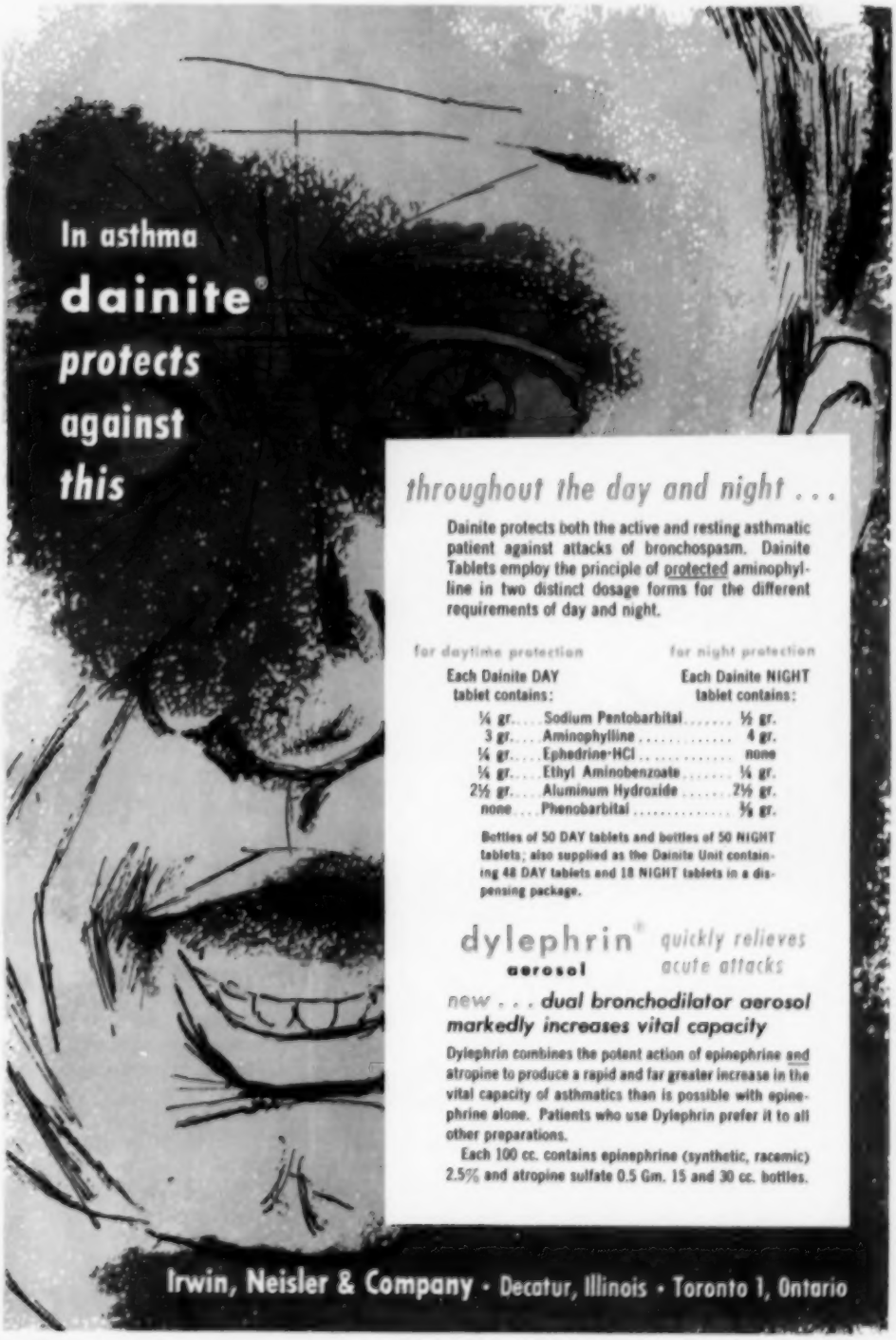

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VOLUME XXVIII AUGUST NUMBER 2

The Clinical Use of Continuous Nebulization in Bronchopulmonary Disease*

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Oakland, California

Introduction

Continuous nebulization therapy describes a new technique in the field of inhalation therapy. The equipment to be presented provides special air conditioning for the control of those factors in the respiratory tract, i.e., retained secretions and local edema, which are frequently responsible for obstruction and deficient ventilation of the lungs. Although the basic mechanical principle, borrowed from standard aerosol therapy, is the addition of microscopic droplets of fluids to the inspired atmosphere, practical features are different in design and function. It is the purpose of this report to briefly outline the physiologic basis, the rationale of the technique and the accumulated clinical experience derived from the several applications of continuous nebulization.

Bronchial Drainage and Mechanism of Obstruction

The bellows action of the muscles of respiration working on the thoracic cage assisted by the distribution system of the tracheo-bronchial tree pumps air in and out of the lungs to supply normal gas exchange to the alveoli.

Narrowing of the tubular distribution system from local edema, bronchospasm or retained secretions may result in deficient alveolar aeration. Propagation or multiplication of this pattern leads to an increase in the physiological dead space of the lung which decreases the efficiency of gas exchange. Allergic sensitivity of the mucous membrane is frequently the basic problem in many cases of bronchial and bronchiolar obstruction. Bronchial spasm, mucosal edema and tenacious mucous plugs are responsible for the rapid onset of obstruction and atelectasis. These factors set the stage for infection and the serious sequelae which follow.

The damaging effect of obstruction of the bronchopulmonary tree is the common underlying factor responsible for the clinical course of a

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large group of respiratory diseases. Three causative factors occurring singly or in combination at several levels in the respiratory tract are frequently responsible for the complications which interfere with normal ventilation. During infection or allergic reaction the pulmonary secretions undergo changes in amount and character. Similar to the response in the nasal passages, there is an increase in the quantity of secretions. In addition, the quality or character of the mucus changes from a thin, clear fluid to an increasingly thick sticky secretion. Admixed with this altered secretion is the outpouring of purulent exudate from the engorged capillary bed. Mucosal edema attends both the inflammatory process or the allergic reaction. When both infection and sensitivity reactions are combined the resulting edema may be out of proportion to the extent of the infection. The increasingly heavy load placed on the cilia to move the abnormal secretions is a third factor in the formation of obstruction. Increased viscosity of the exudate prevents the wave-like motion necessary for movement of the mucous sheath. The moving endless belt system ceases to function because the cilia are stuck down.

Further complications set in as a result of increased respiratory effort. The rate of exchange is increased to maintain the minute volume. Dry outside air robs the mucosa of water vapor aggravating the process of thickening and stasis. These factors play a progressive role in obstruction of the distribution system of the bronchial airways. Edema and engorgement of the vascular bed narrow the lumen of the airway by "inward swelling." Increasing viscosity of the sticky secretions further impedes ciliary function and results in stasis and accumulation. The narrowing process progresses and initially obstructs the bronchioles. Obstruction propagates centrally causing segmental bronchial plugging. Air trapping leads to patchy atelectasis and areas of compensatory emphysema. Each step in this cycle further decreases ventilation and leads to respiratory insufficiency and concomitant hypoxia.

Physiological Basis for Continuous Nebulization

The objective of continuous nebulization therapy is aimed at combating or neutralizing those mechanical factors responsible for obstruction of the bronchopulmonary tree. The return of normal drainage of secretions and the reduction of edema clears the tubular system allowing normal ventilation.

Oxygen is frequently used to increase the pressure gradient across the alveolar capillary membrane. The increased oxygen tension in the alveoli will compensate for deficient ventilation and correct hypoxia. However, Holinger[1] referred to oxygen as an "anti-expectorant." Some of this effect on the respiratory mucous membrane may be due to the low humidity of the compressed gas.

The normal air conditioning system, the nose and nasopharynx, is involved in the process of infection or allergic reaction. In the presence of nasal obstruction the atmosphere entering the bronchial tree is deficient in water vapor. Progressive water loss from the mucous membrane

causes increased viscosity of the secretions. Because the expectorant agents are slow to act and are relatively inefficient, the addition of humidity (water in the vapor phase) to the inspired air or to air-oxygen mixtures has received increasing application in recent years.

With efficient equipment, the inspired atmosphere may be completely saturated with water vapor (100 per cent relative humidity) at room temperature. Under these conditions some water loss from the lung can continue. Because of the difference in temperature between room air and the patient's lung, the atmosphere entering the respiratory tract is elevated to body temperature. At this elevated temperature the original relative humidity is decreased, and water vapor is taken up from the mucous membrane, although to a lesser degree. The problem then is to compensate for this temperature change by supplying an additional source of moisture. The inspired air-oxygen mixture will be more beneficial to the patient if complete saturation is present and it carries additional water in physical suspension. To overcome loss of water vapor from the pulmonary tree and offset the serious effects of local dehydration of the respiratory secretions, a state of "supersaturation" of the inspired air is required.

A gaseous mixture will carry moisture in the form of a fog or mist. This visible cloud is composed of water in the form of microscopic droplets. These nebulized droplets (1 to 10 micra in diameter) will remain suspended in air because of their microscopic size and will not be affected by gravity. This extra quantity of nebulized water is present over and above the water held in the vapor phase. In this way the state of supersaturation desired can be steadily maintained.

On entering the respiratory tract, this mist laden atmosphere supplies the additional water necessary to maintain saturation in the presence of the elevation in temperature. In addition, the great excess of nebulized droplets is carried out to the smallest divisions of the bronchopulmonary tree.[2] As the inspired cloud or fog passes into the branching bronchial tree, the suspended droplets impinge on the interior surface of the walls. In this manner moisture is repeatedly applied to the entire lining of the airways. Thus, the condition of water loss is reversed and is now water gained on the interior surface of the lung. Liquefaction of inspissated secretions occurs progressively and thins the adherent mucus and thick exudate. The lowered viscosity removes mechanical impairment to ciliary function. Accumulated secretions are moved centrally where expulsion is assisted by the tussive squeeze and cough mechanisms.

Additional therapeutic advantage is available by employing the nebulized mist as a vehicle to carry specific medicaments which are active locally on the mucous membranes. Bronchovasoconstrictors added to the water solutions in dilute concentrations will be continuously deposited in the airways to assist in the reduction of mucosal edema. Agents for both local and systemic effect may be absorbed across the intact mucosa. Thus, a physiological method of correcting the common cause of respiratory obstruction is available in the technique of continuous nebulization therapy.

Background and Development of Apparatus and Techniques

The original work in this field of "special air conditioning" was undertaken by physicians who were faced with the problems of obstruction secondary to respiratory infection in the pediatric patient. Pediatricians and otolaryngologists have been aware of the limitations of the "expectorant drugs"[1] and of their inefficiency in maintaining drainage of respiratory secretions.

Atomization of water was initially employed to add moisture to the oxygen tent or "cold steam room." However, this technique produces a spray composed in the majority of large drops such as that generated by a paint spray gun. Large droplet size is not consistent with adequate penetration into the smaller divisions of the bronchopulmonary tree.[2] Also, this coarse spray caused the obvious undesirable, excessive wetting of the patient and his environment without adequate therapeutic results. Investigators turned to the field of aerosol therapy to obtain the nebulizer,

FIGURE 1: Mist O_2 Gen Nebulizer in operation generates nebulized fluid droplets of selected size (80 per cent range from 1 to 3 micra).

a modified atomizer designed to deliver fluids in the form of microscopic droplets. Several reports have been published during the past five yars describing apparatus to accomplish continuous atomization (large droplet size). Further studies revealed the advantages of the smaller fluid particles delivered by continuous nebulization.[3] The apparatus described in these reports have in common either the modification of a medical atomizer to generate a mist of variable size droplets or a method of supplying one of several makes of hand nebulizers with a reservoir supply of fluid for prolonged operation. Several different devices have recently been made commercially available. Hospital and surgical supply houses list several models of equipment to supply "cold fog."

Laboratory and clinical experience in 1949 (Children's Medical Center, Boston)[4] with atomization equipment and also with apparatus which utilized a standard glass or plastic hand nebulizer demonstrated the need for attention directed to optimum standards of construction and performance to be met by equipment for continuous nebulization. Further experience with several types of equipment pointed out the need for an instrument of specific design to meet rigid requirements of performance under hospital conditions. A standardized aerosol composed of true nebulized droplets was desired to meet several clinical requirements. The nebulizer instrument should be designed to:

a. Produce large volumes of nebulized mist.
b. Operate on the usual liters flow per minute of oxygen employed for standard tent or mask techniques.
c. On this oxygen flow the volume of fluid nebulized per unit of time must be more than sufficient for various requirements, i.e., at least 1 cu. ml. per minute.
d. The aerosol produced should consist of fluid droplets of limited size to assure maximum penetration and retention of the fluid throughout the bronchopulmonary tree.
e. Materials for construction of the instrument must be nonreactive with all components of aerosol solutions and must not break down under hard usage and heat sterilization.
f. Gas and fluid jets should be quickly accessible and easily removed to permit clearing of foreign material in the event of clogging.
g. Continuous, reliable performance must be assured without need for constant attention or adjustment by attending personnel.
h. The apparatus should be portable to function in conjunction with all types of inhalation therapy equipment used in modern hospitals.
i. The cost of such an instrument should be within reasonable scale for hospital use.

Because apparatus capable of meeting all these requirements was not available, the assistance of technical engineers was secured for a cooperative project to design and construct a suitable instrument for this purpose. Preliminary work reported in 1951[4] was not successful in adapting a standard nebulizer capable of reliable performance for this special function. Repeated construction of experimental models tested under clinical

conditions resulted in the design of the instrument known as the Mist O_2 Gen® Nebulizer (Figure 1). Over the past 4 years this nebulizer has undergone extensive clinical use for the relief of obstruction of the respiratory tract.[5] Several medical centers employ this instrument for the therapy of respiratory problems in both adult and pediatric patients.

Recently, several new models of aerosol devices have appeared in hospitals. Although each new unit is investigated, the majority of our experience has been with the Mist O_2 Gen instrument. The discussion to follow will, therefore, be concerned with experience derived from the application of this nebulizer to several problems in ventilation secondary to disease of the respiratory tract.

Clinical Applications of Continuous Nebulization Therapy

Bronchopulmonary infection is responsible for a large portion of the morbidity and mortality rate in the pediatric age group. Because of the high incidence of obstruction of the airways secondary to infection and the relatively smaller caliber of the bronchial tree in infants and children, the greatest need for an efficient expectorant is found in this age group. Acute laryngotracheobronchitis, bronchiolitis and aspiration pneumonia respond favorably to a supersaturated atmosphere. Attending otolaryngologists and thoracic surgeons at Children's Hospital of the East Bay have noted a reduction in the incidence of tracheotomy with the use

FIGURE 2: Adaptation of open top oxygen tent for children combined with continuous nebulization. This unit, known as the "Mist O_2 Gen pediatric tent unit" was developed at Children's Hospital of the East Bay to meet standards of efficient operation, patient availability for nursing care and easy portability and storage. The ice cooler and supporting frame are constructed of non-corrosive aluminum alloy. Note the location of the nebulizer suspended from the end of the ice cooler.

of continuous nebulization.[5] A new adaptation of the open top oxygen tent for children was developed[5] (Figure 2) to increase the efficiency of continuous nebulization therapy in terms of high therapeutic concentrations of oxygen combined with the maintenance of a dense nebulized mist. More efficient nursing care and quick access to the patient have benefited the over-all management of these cases.

A special group of the smallest patients, whose lives are frequently endangered by abnormal ventilation, is seen in cases of respiratory distress in the full term or premature newborn infant. Post-mortem examination of neonatal deaths reveal that almost one-half of this infant group dies from abnormal pulmonary ventilation characterized by widespread obstruction of the peripheral respiratory tree.[6] A preliminary report[7] describes the combination of the Mist O_2 Gen nebulizer combined with standard incubator care. Additional experience and supplemental techniques, i.e., postural drainage and sternal traction have proved valuable in the management of these tiny patients.[8] The nebulizer has been used with several types of incubators in medical centers during the past three years.[8] The practical applications of this instrument to the care of premature infants has been described by surgeons[9] and pediatricians.

FIGURE 3: Adaptation of the open top oxygen tent for adult patients. This unit was also developed at Children's Hospital of the East Bay under the supervision of Dr. Paul Samson, Chief of Thoracic Surgery. Design and performance features of the child's unit were modified to accommodate to the teen age group and the adult. Note the adjustable, over-head support from which the tent is suspended permitting the unit to accommodate to any position change of the patient. The flexible plastic material contacts the patient's skin in the area of the shoulder girdle allowing access to all parts for examination or therapeutic procedures.

Medical and Surgical Chest Disease in the Adult Patient

Preparation of older patients for thoracic surgery and treatment in the immediate post-operative period stimulated work with adult cases. Clearing the bronchial tree of retained purulent secretions is of primary importance to the over-all care of these patients. Reduction in the need for repeated bronchoscopy has been one of the consistent results following the use of continuous nebulization.

Acute respiratory infection in military personnel is responsible for a large segment of man hours lost from duty. The Mist O_2 Gen nebulizer was employed in conjunction with a special adaptation of the open top oxygen tent for adult patients (Figure 3) in the treatment of pulmonary complications of upper respiratory infections.[10] Attending medical officers observed early relief of the frequent dry, hacking cough and chest pain. An almost dramatic response was seen in those cases of post-operative atelectasis treated with continuous nebulization therapy. Retained pul-

FIGURE 4A: Mist O_2 Gen nebulizer unit for the tracheotomized patient. The universal clamp and mounting bracket accommodates to all types of tank type respirators and permits installation in a convenient location. The glass jar reservoir may be refilled without removing the nebulizer from the ring support.

monary secretions are not infrequently responsible for serious complications following prolonged anesthesia for extensive abdominal and orthopedic surgery. Prophylactic use of continuous nebulization in the recovery room appears to offer valuable additional care for many surgical patients.

The Tracheotomized Patient

In recent years, tracheotomy has become a safe and reliable procedure in the surgical management of respiratory obstruction. Optimal response follows careful observation of the patient showing signs of obstruction and early use of tracheotomy before the development of irreversible pathological changes.

Several authors advocate the use of humidity in the schedule of after care following tracheotomy to prevent "drying of the pulmonary secretions." Irrigation of the tracheobronchial passages is advised to assist in the removal of crusts and plugs of retained secretions. To prevent pneumonia and to re-expand areas of atelectasis, bronchoscopy through the tracheal stoma is recommended by others.[11] Obstruction of the small caliber bronchi beyond reach of the bronchoscope, is mentioned in a recent report.[12]

The upper respiratory passages normally serve to add moisture and to warm the inspired air. A tracheotomy by-passes this avenue and admits room air directly to the trachea. In this situation moisture is taken up

FIGURE 4B: Close-up view showing the neck mask which surrounds the area of the tracheotomy tube. The transparent plastic cover is in the open position to allow immediate suctioning of the airways.

from the mucosa of the lower trachea and the bronchial tree. Drying of the lining membranes of the entire respiratory tract will progressively increase as a result of this local water loss. A thick, sticky secretion prevents normal function of the cilia causing stasis of secretions, bronchiolar obstruction and atelectasis.

To overcome the air conditioning problems attendant on tracheotomy, the Mist O_2 Gen nebulizer underwent design changes to adapt it for this special purpose[13, 14] (Figure 4, A and B). The use of this instrument* to supply a controlled atmosphere of nebulized moisture to the tracheoto-

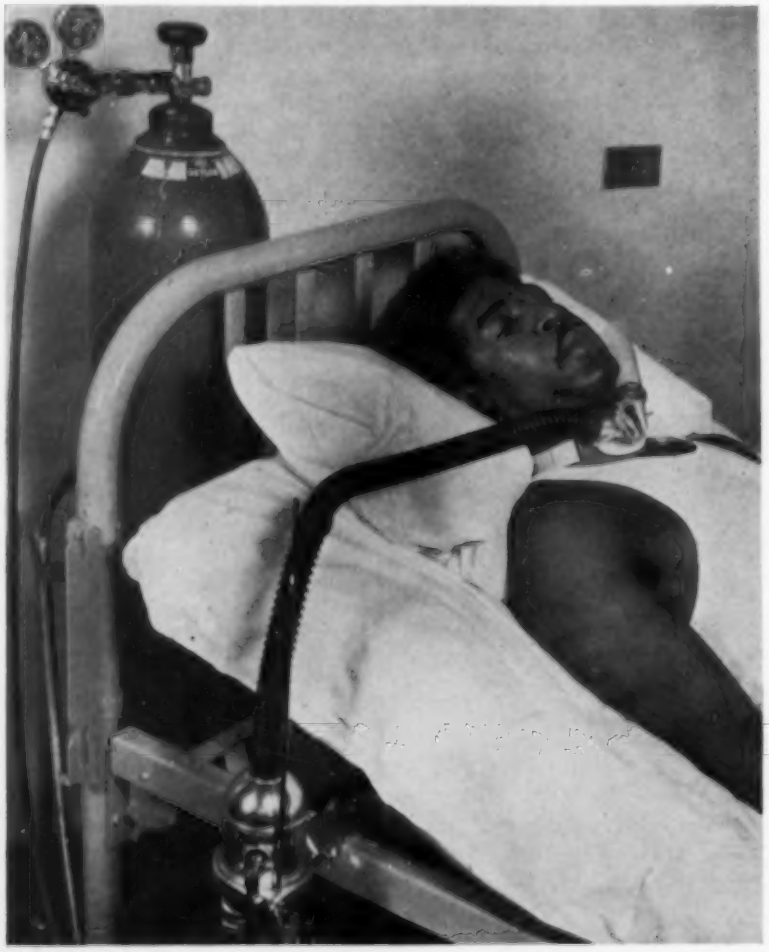

FIGURE 5: Bed patient using Tracheotomy Unit. Note position of nebulizer attached to bed frame. The clamp support may be attached to the verticle member of a movable support stand for intravenous fluids to provide mobility and treatment of several patients.

*The Trach O_2 Mist, Mist O_2 Gen Equipment Co., Oakland, Calif.

mized patient has significantly simplified nursing care and has reduced the pulmonary complications of atelectasis and infection. The equipment is designed to accommodate to tracheotomized bed patients (Figure 5) or those undergoing respirator care.

Composition of Solutions for Nebulization

To accomplish liquefaction and expulsion of retained secretions and to reduce mucosal edema, the fluid vehicle employed for nebulization must penetrate to the far reaches of the peripheral respiratory tract. Our preliminary work included the use of distilled water without additional agents.[4] Abramson[2] has clearly demonstrated that droplets of distilled water will evaporate quickly before reaching the periphery of the bronchopulmonary system. To prevent rapid evaporation of the droplets of water, glycerine is added in concentrations of from 2 to 5 per cent. By altering evaporation a "stable aerosol"[2] is produced which penetrates to the bronchiolar level and beyond to the alveolie. Mechanical addition of fluids occurs by deposition on the mucous membrane. Observation of nebulized mist produced before and after adding small quantities of glycerine to water will demonstrate this physical effect. Increased visibility and prolonged life of the aerosol cloud indicates delayed evaporation.

Propylene glycol possesses similar qualities to glycerine but must be used in greater concentrations to attain similar results. This agent, in addition, has a mild bacteriostatic effect in dilute concentration.

Topical bronchovasoconstrictors assist in controlling mucosal edema, thereby opening narrowed air passages and decreasing the resistance to air flow.[3] Of the several agents used for shrinking the nasal mucosa, we have used ephedrine and Neo Synephrine.[®][7, 8] Both of these agents are capable of undesirable side effects evidenced by vasopressor and central nervous system stimulation. The usual concentration of either neo synephrine or ephedrine is between 0.05 and 0.1 per cent. The reader should recall that continuous nebulization is essentially a new technique. It has been necessary to determine dosage levels on the basis of clinical response to continuous topical administration of agents in dilute concentration. The concentrations are in contrast to the customary use of much greater concentrations locally in relatively larger amounts, for a limited period of time.

Bronchoscopy was performed on a three-year-old child for obstruction of the left main stem bronchus. The area just distal to the carina at the level of the left upper lobe take off was completely occluded by injected and swollen mucous membrane. No cause for this reaction was visible at the first examination. During the following eight-hour period the child was treated with continuous nebulization, the solution contained neo synephrine in 0.25 per cent concentration. Repeat bronchoscopy revealed a marked reduction of the edema with an open bronchus. A smooth white foreign body which proved to be a large bean was protruding from the side of obstruction.

®Winthrop Stearns, Inc.

Although objective measurements are not available at present, the addition of wetting agents to solutions for nebulization appears to speed up the process of liquefaction and mobilization of dry secretions. Where areas of atelectasis are present, a known surface tension exists in the interface between mucous membranes in contact. The major force resisting aeration of atelectatic areas is said to be "cohesion of moist surfaces." Local concentrations of a wetting agent at the site of atelectasis will reduce surface tension in the area of contact between mucous membranes. Objective proof of the importance of surface tension and evidence for the effect of "surface-active substances" on cohesive forces is presented in a report by Gruenwold.[15] Clinical and laboratory studies on several wetting agents were done to determine their relative efficiency in reducing surface tension and their toxicity to animals and man.[16] At present, the agent of choice is a nonionic substance (alkyl-aryl polyether alcohol) known as Triton WR-1339.* Concentrations used for continuous nebulization are from 0.025 to 0.125 per cent. Detergent solutions are employed for those cases where tenacious gummy secretions or atelectasis complicate the picture of obstruction.

It is unusual to add antibiotics to the solution for continuous nebulization. In some cases of overwhelming infection in the pediatric group or

FIGURE 6: Intermittent aerosol treatment using the Mist O_2 Gen face mask unit. The nebulizer is attached to a portable "I.V. Stand" by the universal clamp and ring support bracket. The expiratory valve in the face mask is directly under the patient's index finger.

*Rohm and Haas Co., Philadelphia, Pennsylvania.

for cases of chronic pulmonary suppuration, a high local concentration of penicillin, streptomycin or both may be effective where systemic blood levels do not reach the site of infection in sufficient concentrations. Crystalline soluble penicillin and streptomycin have been used in concentrations of 1 million units and 1 gram, respectively, per 100 ml. of solution.

Discussion

The Mist O_2 Gen instrument was developed to answer a widespread need for heavy concentrations of mist of limited droplet size. Because the cubic volume of the oxygen tent or hood surrounding the head of the patient is not the same in all instances, the nebulizer was designed to produce a heavy concentration of aerosol. Even when using low oxygen flows, (4 liters per minute) an effective concentration of nebulized mist is maintained.

This property of heavy concentration or large volume output is probably responsible for the beneficial results observed in the case of the tracheotomized patient. Several physicians have noted the rapid response evidenced by thinning of secretions and clearing areas of atelectasis. Similar treatment using the small type of hand bulb nebulizer was technically difficult and not always successful after prolonged periods of therapy.

To make this heavier concentration of aerosol available to patients using intermittent aerosol therapy, the directional flow Mist O_2 Gen Nebulizer from the tracheotomy unit was adapted for a new function (Figure 6). The distal end of the flexible conduction tube is fitted with a face mask** containing sensitive inspiration and expiration valves. This apparatus is used for administering aerosol treatments to hospital and home patients. Occasionally it is beneficial to "taper off" continuous nebulization with an intermittent schedule of 20 minutes of nebulization every three hours using the mask unit at the bedside.

Patients with chronic bronchial asthma complicated by emphysema and fibrosis may be seriously incapacitated by retained secretions. Some patients in this group have received marked benefit from a schedule of nebulization in the home or at work employing the Mist O_2 Gen unit operated from an oxygen or compressed air cylinder. These patients had previously used the standard type hand nebulizers operated with oxygen. The use of detergent aerosol solutions may be partially responsible for the observed changes, however, the increased concentration of aerosol and the ease and facility experienced with the mask unit must play a significant role.

Intermittent positive pressure breathing therapy is receiving increasing recognition in the treatment of chronic bronchopulmonary disease. Increased and more efficient alveolar aeration and improvement in maximal breathing capacity frequently results from its use. Preliminary experience has shown promising response to a schedule of continuous nebulization combined with short periods of positive pressure breathing. Although little experience is available to date, the pediatric patient suffering from severe asthma appears to be an excellent candidate for this combined

**Bennett Oxygen Therapy Mask, V. Ray Bennett, Los Angeles, California.

approach. Drainage of their thick secretions and assistance with ventilation are equally beneficial for these small patients.

Bower and associates[17] have demonstrated increased ventilation of the tracheotomized respirator patient using the Bennett Positive Pressure Respirator attachment for the tank type respirator. In those cases where this method of "combined pressure breathing"[17] is used, bronchial drainage will be increased by the addition of nebulized fluids to the oxygen-air mixture delivered to the lungs. A recent model of the Mist O_2 Gen instrument is designed to function in the line of the positive pressure system (Figure 7). As each surge of air is delivered in time with the inspiratory

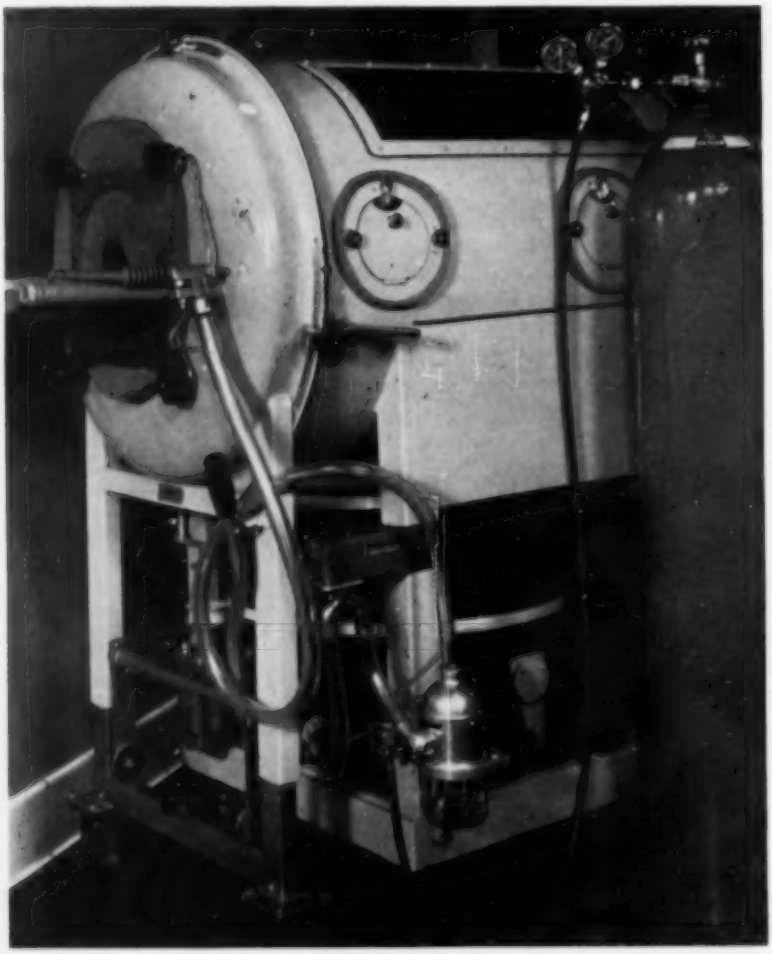

FIGURE 7: Special adaptation of the Mist O_2 Gen nebulizer incorporated in the outflow circuit of the Bennett Positive Pressure Respirator attachment. This unit, as shown on a Drinker Collins Respirator, will add nebulized fluids as needed to the positive pressure flow and remain in place when not in use.

cycle, it passes through the Mist O_2 Gen nebulizer. In this interval the air is charged with a concentration of nebulized mist. With this combination the optimum quantity of aerosol is distributed to the site of infection or obstruction.

More efficient distribution of aerosols is one of the major therapeutic aims of positive pressure breathing equipment. The same air or oxygen flow which benefits the patient with increased residual lung volume also assures penetration of aerosol droplets into the peripheral areas of the bronchopulmonary tree. The Mist O_2 Gen instrument adapted for positive pressure has undergone initial trial attached to the gas flow circuit of the Bennett Pressure Breathing Therapy Unit* (Figure 8). This adaptation supplies increased concentrations of detergent aerosol solutions of controlled particle size in combination with flow sensitive pressure breathing. The clinical value of this additional feature will be determined only after experience with a large group of patients.

The clinical applications of continuous nebulization therapy presented in this discussion have evolved directly from problems met at the patient's

FIGURE 8: The Bennett Pressure Breathing Therapy unit combined with the Mist O_2 Gen nebulizer to deliver greater concentrations of therapeutic aerosols to the bronchiolar area. Note the rubber stopper closing the manifold port where the small hand nebulizer is inserted.

*V. Ray Bennett & Associates, Los Angeles, California.

bedside. The cooperation of engineering talent has provided the clinician with instruments to assist in the maintenance of an open airway and support of normal ventilation. Since the initial work on this project in the field of acute respiratory disease in children, the application of the original technique has extended to the adult patient and to specialized treatment problems. New fields of application are under investigation in local hospitals.

During prolonged surgical procedures, the anesthesiologist may be concerned with retained pulmonary secretions. Adequate suctioning through the endotracheal tube will maintain a clear airway in the great majority of cases. Occasionally thickened secretions are not easily cleared from the airways especially when they collect in segmental bronchi or further out in the smaller divisions. The introduction of carefully controlled quantities of nebulized fluids in the gas circuit flowing to the patient will minimize the drying factor of anesthetic gases and assist in clearing the airways. The Mist O_2 Gen unit for positive pressure will accommodate to the conduction system of anesthesia apparatus permitting the anesthetist to deliver controlled periods of nebulization in the anesthetic gas when needed.

Chemical and thermal injuries to the tracheobronchial tree cause acute inflammatory reactions. Edema and exudate may quickly obstruct the respiratory tract. In times of national emergency, the care of patients in acute respiratory distress will hold the highest priority and responsibility for all physicians. Those physicians active in the field of chest disease should be equipped to meet such emergencies with advanced techniques to support respiration under difficult conditions until hospital care is available.

The pathological picture in cases of flame injury to the respiratory tract closely resembles that of acute tracheobronchitis. This reaction, characterized by intense congestion, edema and exudate, was found in victims of the Coconut Grove disaster.[18] Heavy concentrations of smoke or airborne toxins would be likely to cause similar reactions. Portable equipment for combined nebulization—oxygen therapy designed to function in the emergency situation is now in the developmental stage. With such equipment available for instant use the progressive changes leading to peripheral obstruction and irreversible damage could be modified or prevented.

The efficiency of any therapeutic technic is directly in proportion to the knowledge and skill of those directing its use. Experience in the role of "trouble shooter" in the field of inhalation therapy repeatedly demonstrates a rather frequent lack of knowledge on the part of attending physicians of basic principles or limitations of the technique as applied to individual patient care. Emphasis should be placed on the preparation of specific prescriptions for aerosol solutions for each individual case. No one prescription or stock solution will assure good results with continuous nebulization. Equipment for nebulization therapy should receive the attention and care which is routinely given to anesthetic apparatus.

Conclusion

The writer has attempted to present the physiological background and practical aspects of what is essentially a new approach to the management of bronchopulmonary disease. With proper attention to the details of technique, preparation of solutions for nebulization and methods of administration, continous nebulization therapy becomes a successful procedure worthy of continued study and widespread application.

The project presented in this report was initiated under the sponsorship of Dr. Robert E. Gross, William E. Ladd, Professor of Children's Surgery, The Harvard Medical School, and with the active cooperation of Dr. Robert M. Smith, Director of the Department of Anesthesia, Children's Medical Center, Boston.

Dr. Chester M. Weseman, Chief of Otolaryngology, Dr. Paul C. Samson, Chief of Thoracic Surgery, and Dr. J. Hallam Cope of Children's Hospital of the East Bay, Oakland, are responsible for suggestions on clinical applications and the sponsorship which made it possible to continue investigation in our local hospitals.

The development of the medical equipment described could not have been accomplished without the generous efforts of the consultant engineers from Production Foundry Company, Oakland, and their successors Mist O_2 Gen Equipment Company, who gave unlimited time to the several technical problems and also furnished funds to support the clinical studies.

SUMMARY

1. The mechanisms of respiratory tract obstruction and the serious sequelae are reviewed. The physiological basis and therapeutic rationale of continuous nebulization therapy is presented as a method to correct the factors responsible for obstruction.

2. Clinical applications of equipment for continuous nebulization applied to adult and pediatric medical and surgical chest disease are presented to illustrate the practical value of this therapy.

3. Components of solutions for nebulization therapy are discussed in relation to their function in the control of respiratory obstruction.

4. Recent developments in therapeutic combinations of positive pressure breathing and nebulization are described.

5. The techniques presented may serve to provide immediate support for pulmonary emergencies during a period of national disaster.

RESUMEN

1. Se revisa el mecanismo de la obstrucción de la obstrucción del conducto respiratorio y las serias consecuencias de él. Se presentan las bases fisiológicas y terapéuticas racionales para la nebulización contínua como un método para corregir los factores que producen la obstrucción.

2. Para ilustrar el valor práctico de este tratamiento se presentan las aplicaciones clínicas del equipo para la nebulización contínua en el adulto y en el niño, así como en cirugía del tórax.

3. Se discuten los componentes de las soluciones para nebulizaciones.

4. Se hace una descripción de los progresos recientes en el tratamiento por nebulizaciones combinado con inhalaciones apresión.

5. Las técnicas presentadas pueden servir para coadyuvar inmediatamente con las medidas de emergencias pulmonares en caso de desastres nacionales.

RESUME

1. L'auteur passe en revue les mécanismes de l'obstruction des voies respiratoires et leurs séquelles graves. Il expose les bases physiologiques et thérapeutiques de la nébulisation continue comme méthode propre à corriger les facteurs responsables de l'obstruction.

2. Il rapporte, pour illustrer la valeur pratique de ce traitement, les applications cliniques de l'appareil à nébulisation continue destiné aux affections pulmonaires médicales et chirurgicales de l'adulte et de l'enfant.

3. Il discute la composition des solutions pour nébulisation en fonction de leur action dans le traitement de l'obstruction respiratoire.

4. Il décrit les récents progrès des combinaisons thérapeutiques de la respiration en pression positive et de la vaporisation.

5. Les procédés exposés peuvent servir à apporter un secours immédiat dans les urgences pulmonaires en cas de catastrophe nationale.

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Alterations in Lung Function and Anatomy in Heart Failure with Particular Reference to Mitral Stenosis*

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The unique position of the pulmonary circulation, lying between the right and left side of the heart, leads commonly to involvement of the lungs when there is disturbed cardiac function, and to cardiac failure when there is disordered anatomy and function of the lungs. It may often be difficult to assess which is the primary disturbance; and, indeed, since a wide variety of symptoms such as dyspnea, orthopnea, chest pain, hemoptysis and diminished exercise tolerance are common to both cardiac and pulmonary disease, a problem in differential diagnosis frequently is presented. We are concerned here with the effect of cardiac disease on lung anatomy and function, and the mechanism by which these changes take place.

Pulmonary Hypertension

The characteristics of the pulmonary circulation are quite distinct from those of the systemic circulation. Whereas the latter is a high pressure system with numerous homeostatic controls via reflexes (e.g. aortic and carotid), the pulmonary circulation is a low pressure system, the control of which is not as well defined. Pulmonary artery pressure is determined by the pulmonary blood flow, the capacity of the pulmonary vascular bed, and finally by the pressure in the left atrium.[1] A significant increase in any of these factors may elevate pulmonary artery blood pressure. For example, increased pulmonary flow up to 2.5 to 3 times the normal in a healthy individual will produce no rise in pressure[1] but larger increases in flow, such as encountered in patients with patent ductus arteriosus may produce pressure elevations.[2] The increased pulmonary artery pressure in turn may lead to pulmonary arteriosclerosis and anatomical changes in the pulmonary vessels, which produce an additional rise in pressure.

Restriction in capacity of the vascular bed may also lead to pulmonary artery pressure elevation, as occurs in cor pulmonale secondary to chronic pulmonary emphysema, silicosis, sarcoid, mitral stenosis, etc.[1,3] Apart from organic restriction, the role of anoxia in reducing capacity of the pulmonary vascular bed and increasing blood volume and cardiac output, all of which accentuate pulmonary hypertension, must be borne in mind, particularly in the case of chronic pulmonary emphysema.[3]

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The most important factor in producing pulmonary hypertension from the standpoint of the present discussion is elevation of the left atrial pressure. Such an elevation may result from rheumatic mitral valve disease or failure of the left ventricle, regardless of etiology. Under such circumstances the pulmonary vascular bed becomes distended, and if the pulmonary capillary pressure rises excessively, transudation may occur and lead to pulmonary congestion, characterized by rales at the lung bases or indeed, by massive pulmonary edema requiring urgent therapy. Hypertension in the pulmonary artery is increased by local arteriolar constriction which causes a reduction in vascular capacity. This pulmonary arteriolar narrowing may indeed be reflected in the organic changes found in postmortem or biopsy examinations of the lung.[4]

Changes in pulmonary circulation have a profound effect on pulmonary function. Respiratory difficulty may further be magnified if elevation of systemic venous pressure is present also, producing pleural effusion[5] or ascites. Finally, enlargement of the heart may further compromise pulmonary function, because the expansion of cardiac volume in the semirigid thoracic cage must be at the expense of lung volume.[6]

Alterations in Lung Volume

Alterations in the lungs produced by left-sided heart failure of any cause and by mitral stenosis without congestive failure are similar in many respects and differ in others. Numerous studies have been made of the effect of these conditions on lung volume.[6,7] In general, it has been found that the vital capacity is reduced,[6-11] the degree of reduction being partly related to the severity of the failure. The components of the vital capacity, namely, expiratory reserve volume and inspiratory capacity, have been reported to be decreased.[12] The recent study of Frank and co-workers[13] demonstrated that there was a symmetrical reduction of the inspiratory capacity and expiratory reserve volume in all stages of disability.

Before heart failure sets in the total capacity of the lungs is unchanged or only slightly decreased due to impaired distensibility and increased cardiac size. As congestive heart failure ensues the lung volumes are less than their immediately preceding values.[6-8] Richards and co-workers[6] demonstrated also an elevated resting level of respiration, a slight decrease in expiratory reserve volume and a slight increase in the functional residual volume and residual volume (noted also by Christie and Meakins[14]) in the presence of congestive heart failure. They further observed that with increasing severity of failure the residual volume and functional residual volume are decreased sharply, a finding observed previously.[12] In contrast to these studies, West and others[15] have shown that there may be no appreciable alterations in the lung volumes even in the presence of severe pulmonary vascular engorgement, provided that pulmonary edema or hydrothorax are absent.

The factors leading to the reduction in vital capacity and other lung volumes include increased pulmonary blood volume with reduced distensibility of the lung, increase in cardiac size in general, and of the left atrium in particular in mitral stenosis, and further pulmonary compression caused

by ascites or pleural effusion which are sequelae of increased systemic venous pressure. The changes in total capacity are accounted for by similar mechanisms. These changes parallel closely those of vital capacity although they are not as marked; that is, they are not significantly altered or only slightly reduced.

In general, as has been noted, the changes in lung volume correlate with the degree of cardiac failure. In the case of mitral stenosis there may be no change at all in the lung volumes in the absence of cardiac failure or even when pulmonary vascular pressures are elevated and diffusing capacity impaired, but vital capacity is reduced when ventilation-perfusion relationships are abnormal with increased dead space ventilation.[16]

The bellows function of the lungs in congestive heart failure and mitral stenosis, as measured by maximum breathing capacity, is also impaired[13, 17-19] commonly being slightly reduced. In pulmonary emphysema on the other hand, there is marked reduction in maximum breathing capacity which is one of the physiological hallmarks of the disease.[20] Maximum expiratory effort is only minimally delayed even when wheezes and rales are present. In cases of mitral stenosis it has been demonstrated that there is a decrease in the maximum tidal volume[13] but no large increase in the total resistance of the tracheo-bronchial tree and tissue resistance.[21] Indeed, the spirogram usually shows no trapping or obstruction. In view of the absence of significant obstruction, the factor responsible for the reduction in maximum breathing capacity (when it occurs) is probably muscular fatigue. Such a reduction, together with the hyperventilation so common in heart failure, leads to a decrease in breathing reserve.[17, 18] In the most recent study,[15] the reduction in breathing reserve was not marked. Alterations in the breathing reserve are not sufficient to explain the dyspnea so commonly encountered in patients with mitral stenosis or congestive heart failure. This has led to investigation of abnormalities in mechanics of breathing in such patients, in order to evaluate their possible role in producing dyspnea.

Pulmonary Compliance and Resistance

Evaluation of pulmonary mechanics by more refined techniques has received great attention in recent years.[21-26] The work of breathing is performed against a variety of resistances. These include: resistance due to the elastic properties of the lungs, air viscance and turbulence, and resistances associated with tissue deformation. While analysis of these factors individually is possible, in practice only two types of resistance are measured. The elastic property of the lung is expressed in terms of pulmonary compliance (a measure of the "stretchability" of the lungs) and varies inversely with the elastic resistance of the lungs. All other resistances (air turbulence and viscance and tissue viscance) are considered together and expressed as pulmonary resistance.

It has been demonstrated that in normal subjects, the pulmonary compliance correlates directly with vital capacity, body height and surface area.[24] Pulmonary resistance varies inversely with and is less significantly

related to these measurements. In patients with rheumatic heart disease, in whom mitral stenosis is the predominant valvular lesion, pulmonary compliance is significantly reduced.[21] While this reduction has been noted in patients with rheumatic disease with or without heart failure the reduction is much greater in the former group.[21] Reduction in compliance may be present in patients who have no significant disability and in whom routine ventilatory tests are normal.

Pulmonary resistance is increased slightly in patients with mitral stenosis, the increase being more marked when congestive heart failure is present. Increment in pulmonary resistance in patients with compensated heart failure is not associated with abnormalities in conventional ventilatory tests (e. g. maximum breathing capacity and timed vital capacity). Even when circulatory failure is present and pulmonary resistance is definitely increased (but much less so than in pulmonary emphysema) conventional ventilatory studies are not significantly altered, although they may suggest changes in airway resistance. The observations of Mead et al[21] have been confirmed by Marshall, McIlroy and Christie.[26] It should be noted that Christie and Meakins[14] had studied the problem of increased rigidity of the lungs in cardiac failure more than 20 years ago. They found intrapleural pressure swings during quiet respiration to be much greater in patients with congestive failure than in the normal. They concluded, therefore, that increased rigidity of the lungs existed. Marshall and co-workers confirmed the reduction in compliance, and noted also greater reduction (i. e. even more rigid lungs) during exercise.[26]

From these physical studies of the work of breathing it is possible to determine the minimum work required for a given alveolar ventilation.[23, 25] In patients with mitral stenosis, not only does the degree of dyspnea and orthopnea correlate well with the increase in rigidity of the lungs (as reflected in increased total work and reduced pulmonary compliance) but also, there is an increase in optimum frequency of respiration for minimum work for a given alveolar ventilation. Marshall and others[26] offer this as a basis for the shallow rapid respirations of the patient with mitral stenosis with respiratory difficulty.

Measurement of the work of breathing has not only been evaluated by these physical techniques, but also by measurement of oxygen consumption during hyperventilation. In general, in patients with diffuse lung disease as well as heart failure due to mitral stenosis, there is greater energy required for a given minute ventilation as compared with normal subjects. In two cases of mitral stenosis, the increment in oxygen consumption during hyperpnea for one patient with considerable respiratory difficulty was similar to that found in a case of severe pulmonary granulomatosis, while in a second case with definite mitral stenosis (proved at autopsy) and minimal symptoms of respiratory difficulty, the increment in oxygen consumption was about normal.[27]

It is important that in cases of mitral stenosis, with increased need for oxygen during exercise, there is inability to adequately increment cardiac output, hence the normal integrated response to exercise fails.

Distribution of Gases and Diffusing Capacity

Distribution of gases in the lungs in cardiac failure was found by earlier workers to be abnormal.[7] Cournand and others[28] found it to be normal. Of 22 patients with mitral stenosis recently studied by Carroll, Cohn and Riley, there were six with diffusion difficulties. They found a high dead space-tidal ratio, i. e., a reduced effective alveolar ventilation. The increases in dead space ventilation correlated well with reduction in vital capacity and indicated, perhaps, that both relate to vascular congestion and edema. This is supported by the fact that in three patients with mitral stenosis, commissurotomy resulted in an increase in vital capacity and maximum breathing capacity and reduction in dead space ventilation.[16]

The abnormalities in distribution account for only a small increase in venous admixture[16] which may be accompanied by a slight reduction in arterial oxygen saturation at rest. Ordinarily, in mitral stenosis or in congestive heart failure, arterial oxygen saturation at rest is not reduced significantly, although it has been reported to be slightly reduced by several observers.[7] If significant arterial unsaturation occurs at rest, pulmonary involvement due to edema, infarction or pneumonia should be sought. Cyanosis, on the other hand, is fairly common, but often reflects increased arteriovenous oxygen difference with unsaturated venous blood in the subpapillary venous plexus.[7] Small reductions in arterial oxygen tension do occur commonly but are not associated with changes in arterial oxygen saturation because of the shape of the oxyhemoglobin dissociation curve. Such reduction must be measured by direct determination of arterial oxygen tension. Studies at one level of oxygenation by Blount and others[29] demonstrated that at rest the group of patients with mitral stenosis had a normal alveolar oxygen tension and a reduced arterial oxygen tension, with a resultant increase in the alveolar-arteriolar oxygen gradient compared with control patients. With exercise the alveolar oxygen tension rose in both groups (rheumatic heart disease and controls) with essentially no change in the arterial oxygen tension. Carroll et al[16] have carried out similar studies, employing the technique devised by Riley and Cournand[30, 31] for the study of patients at two levels of oxygen breathing, and have shown an increase in the alveolar-arterial gradient in some cases, while breathing room air and also during moderate anoxia.

Such studies demonstrate not only distribution difficulty in mitral stenosis but also abnormalities in diffusion. Of the 22 cases noted above, there were six with pure diffusion difficulty and 10 more with combined diffusion and distribution abnormalities. In the latter group, eight of 10 patients had elevated pulmonary artery pressure at rest, and five of six had increase in pulmonary capillary pressure. All had severe dyspnea. Reduction in diffusing capacity was noted in 16. Such a reduction is ordinarily attributable to decrease in diffusing area or to alteration in the diffusing surface of the lung. Carroll et al[16] point out that an alteration in the diffusing surface in mitral stenosis is suggested but not proved by the anatomical studies of Parker and Weiss.[4] As to whether there are physico-

chemical alterations in the diffusing surface, no statement can be made. Insofar as reduction in diffusing area is concerned, some support from the studies of Parker and Weiss[4] is available. Direct count by these authors seemed to show a reduction in the number of pulmonary capillaries as as a result of degenerative changes secondary to prolonged pulmonary capillary hypertension. Not only may there be an anatomical reduction in diffusing area, but also a functional one, as indicated by the fact that the diffusing capacity normally increases with exercise, suggesting that certain capillaries open to receive the increased pulmonary blood flow. Indeed, the diffusing capacity reached during exercise is a more critical measure of impairment of this function.[32] In mitral stenosis, failure to increase the cardiac output may be responsible for a much lower diffusing capacity during exercise, compared with control subjects who are able to increase their cardiac output to greater levels.

Anatomical Changes in the Lungs

From the physiological disturbances described we see that the cycle of events starting with elevation of left atrial pressure is one in which profound functional alterations may ensue. Should sustained elevation of pressure persist, anatomical changes may also appear.

The observation of large swollen and congested lungs in patients dying of congestive failure called attention in the early pathological studies to the anatomical alterations secondary to chronic passive congestion. Congested blood vessels, transudation into the alveoli and the appearance of phagocytes containing inclusion material and debris of hemosideral nature, the so-called "heart failure" cells, are the characteristic anatomical findings. Protracted pulmonary hypertension may also be accompanied by atheromatous changes in the larger pulmonary vessels.

In the event that mitral stenosis is the underlying heart lesion, the pathological changes in the lungs are more striking. It was Parker and Weiss[4] who called attention to the extensive morphological change in the pulmonary vasculature. Apart from pulmonary edema, they reported dilatation of the pulmonary capillaries with thickening of the capillary basement membrane, as well as collagenous thickening of the alveolar walls. These changes were particularly prominent in the lower lobes. Reduction in the total number of capillaries was also found. Furthermore, they noted the presence of hyperplastic arteriosclerosis and intimal arterial thickening. Alterations in the pulmonary arterioles were further emphasized by Larrabee, Parker and Edwards,[33] as consisting of thickening of the medial musculature as well as in intima. These findings were confirmed by Graham and co-workers.[34]

More recent studies by means of lung biopsy[35] revealed that in 32 patients with mitral stenosis, there was hypertrophy of the arteries and arterioles in 11 cases. Sclerotic changes were present in the form of irregular intimal thickening or gross adventitial thickening (six cases). Necrotizing arteritis was present in one case in which the pulmonary artery pressure was 65 mm. of Hg. In some instances, intimal thickening

was related to elastosis with intraarterial thrombi. No calcification or atheromatous plaques were seen, nor was there evidence of bronchopulmonary anastomoses. The ratio of the lumen to wall was at most 4:1 in patients with mitral stenosis. Larrabee, Parker and Edwards[33] described the normal ratio as 5.5:1 to 10.3:1 for a normal necropsy specimen. Therefore, the lowered ratio in mitral stenosis seems significant. Furthermore, the greater the systolic, diastolic and mean pressures, the smaller was the mean arteriolar ratio (lumen:wall).

One may ask if these anatomical alterations are reversible when the left atrial pressure is lowered by successful mitral commissurotomy. Long-term comparison of tissue specimens obtained at operation and subsequent necropsy or biopsy and long-term serial cardiac catherization studies should provide us with an answer to this vital question.

Apart from vascular alterations secondary to rheumatic mitral disease the pathological sequelae of the connective tissue and vascular disturbance which characterizes active rheumatic fever leave their scars in the lung, pleura and pericardium. In the acute phase, pain or effusion due to pleuritis may diminish pulmonary excursion, with decreased tidal air and vital capacity. Pulmonary perenchymal involvement in the form of "rheumatic pneumonia"[16, 37] with involvement of the alveoli is still a controversial question. It is seen in 10 per cent of the cases of rheumatic fever.[36] When it occurs, usually in severe cases, it is accompanied by dyspnea and cough with little or no sputum, in the absence of commensurate physical findings in the chest. Pathologically, there may be angiitis of an "allergic type" with endothelial proliferation, hemorrhage, and necrotic changes. Aschoff bodies may also be found. Clinically, these changes may appear as multilobular areas of patchy density which are usually evanescent. Occasionally, the areas may go on to calcification and even ossification.[38]

Alveolar changes of a more permanent nature are usually encountered, with fibrosis of the alveolar walls and changes in the capillary structure (as noted above). Diapedesis of red cells and deposits of hemosiderin in the alveoli lead to the picture of hemosiderosis often marked enough to be seen on x-ray examination.[39] Calcification in these areas of hemosiderosis may occur. Differentiation from the calcification of pulmonary tuberculosis is readily apparent from the associated severe rheumatic mitral stenosis and abnormal configuration of the heart, as well as the more frequent basal location of these calcifications in contrast to tuberculosis.

Hemoptysis in mitral stenosis is usually due to pulmonary congestion and varicosities of the bronchial veins.[40] It should be noted that the anastomoses between the pulmonary and systemic vascular systems favor formation of these varicosities. If bleeding is significant, blood pneumonias may appear. Hemoptysis may herald a pulmonary infarction which is frequent in mitral stenosis and indeed in heart failure of any etiology. The sites of origin of the pulmonary emboli are either the leg veins or occasionally the right auricle. Pulmonary infarction is more apt to occur if there is embolization to a previously congested pulmonary vascular

tree (as proved both clinically and experimentally).[41] The usual picture of acute chest pain, hemoptysis, pleuritic pain, hemorrhagic pleural effusion, and x-ray signs of pulmonary infiltration which is usually peripheral and wedge-shaped, or of plate like linear areas of atelectasis, make the diagnosis easy, but variations in this clinical picture may occur which are less classical and more difficult to recognize.

Alterations in the bronchi are not common. Varying degrees of elevation and pressure on the left main bronchus, while a diagnostic finding during fluoroscopic examination, rarely produce clinical changes. Rarely, pressure from an enlarged left atrium may lead to partial bronchial obstruction with bronchiectasis secondary to the infection which follows the obstruction. Hemoptysis from such a source, while extremely rare, may present a difficult diagnostic problem. Uncommonly, pressure on the right middle lobe bronchus may be seen and a single instance of collapse of this lobe has been reported.[42] More commonly pressure on bronchi produces spasmodic coughing episodes which may be relieved by decongestive measures.

Occasionally, a localized interlobar effusion due to congestive heart failure may appear on a chest roentgenogram and be difficult to differentiate from neoplasm, infarction, or tuberculosis.[43, 44] This was noted in about 0.22 per cent of a large series of isolated lesions in the lung. Its presence can usually be suspected in a patient who has an enlarged or abnormal cardiac silhouette and a density in the area of one of the interlobar fissures. Lateral chest films often help determine whether the localized collection of fluid is actually in the plane of a fissure. Vigorous treatment of the cardiac failure is indicated from both therapeutic and diagnostic standpoints, since such lesions will usually disappear promptly following adequate therapy for congestive failure.

SUMMARY

The effects of cardiac disease on the lung have been discussed with particular references to the congestive failure state. In addition, those factors peculiar to rheumatic heart disease, when it is the cause of this failure, have been emphasized. The sequence of events starts with elevation of the left atrial pressure, leading in turn to changes in the pulmonary hemodynamics and pulmonary blood volume. These in turn produce changes in the pulmonary ventilation perfusion relationships which have been described. The complicating anatomical alterations which are secondary to the pressure alterations have also been discussed.

RESUMEN

Se discuten los efectos de la enfermedad cardiaca sobre el pulmón de manera especial refiriéndose al estado de insuficiencia congestiva. Además, se recalcan los factores peculiares a la enfermedad cardiaca reumática cuando es la causa de esta insuficiencia. La secuela de sucesos empieza con elevación de la presión atrial izquierda conduciendo después a cambios en la hemodinámica pulmonar y en el volumen de la sangre pulmonar.

Esto a su vez, produce cambios en la relación entre el volumen pulmonar y la ventilación pulmonar que se han descrito. Las alteraciones anatómicas complicantes que son secundarias las alteraciones de presión también se discuten.

RESUME

Les auteurs discutent les effets des affections cardiaques sur le poumon, en insistant particulièrement sur la congestion due à l'insuffisance cardiaque. En outre, ils montrent les éléments particuliers du rhumatisme cardiaque, lorsqu'il est la cause de cette insuffisance. Le processus commence avec l'élévation de la pression artérielle gauche, entrainant à son tour des modifications de l'hémodynamisme pulmonaire ou du volume sanguin du poumon. Ces phénomènes à leur tour entrainent des altérations des volumes pulmonaires et des rapports qui les unissent à la ventilation pulmonaire. Les auteurs mettent également en discussion les altérations anatomiques secondaires aux modifications de la pression.

Complete reference list will be published in reprints.

Esophageal Motility in Health and Disease*

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The development of small sensitive pressure-detecting devices for the accurate and continuous registration of esophageal pressures has revived interest in the mechanism of deglutition in the normal man and in his disease states. As a result of the application of these new techniques to the study of esophageal motility and the correlation of physiologic, pharmacologic, and anatomic data, new interpretations of dysphagia in certain disease states are now available. It is the purpose of this paper to review these newer developments as they pertain to esophageal motility in health and disease.

Methods for Studying Esophageal Motility

Until recently, the two methods most frequently used to study esophageal motility and the effect of pharmacological agents were roentgenologic techniques and methods employing balloons to obtain kymographic records of esophageal motor activity. The advantages and limitations of these methods have been discussed previously.[1]

Roentgenologic methods must, of necessity, be employed during brief periods of observation, and continuous records of motor activity are difficult to obtain. For visual interpretation of the dynamics of deglutition, however, roentgenologic techniques are unsurpassed.

Balloon methods for studying esophageal motor activity offer the advantage of prolonged periods of observation, and they are easily adapted to the continuous recording of motor activity. The disadvantage of this method is that the balloon must be expanded if changes in its volume are to be recorded. The filling of a balloon with air or water under positive pressure results in distention of the esophagus where intraluminal pressure is normally negative. The resulting distention thus provides a local stimulus for motor activity. Although modifications of the balloon method have been used to excellent advantage in studies of the effects of various pharmacologic agents on the esophageal musculature,[2, 3] definite limitations in recording motor activity resulting from deglutition exist. The balloon, which is anchored at one site, acts as an obstruction to the swallowed liquid or bolus. The almost continuous activity which the balloon stimulates interferes with the recording of sequential motor activity resulting from deglutition.

By new techniques,[4, 5, 6] it is now possible with miniature pressure transducers or small open tipped tubes to record, accurately and continuously, changes in esophageal intraluminal pressure resulting from motor activity. These methods do not obstruct or stimulate the esophagus.

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Following deglutition, pressure changes occurring in different levels of the esophagus can be recorded with ease.

Stages of Deglutition

As stated by Starling,[7] "It has been customary since the time of Magendie to divide the act of swallowing into three stages." The first stage is a voluntary act which initiates the other two stages, which are reflex in origin. In the first stage, liquid or a bolus of food is passed from the mouth into the pharynx. This is accomplished principally by the mylohyoid muscles which retract and elevate the tongue against the hard palate, thus forcing the liquid or bolus into the pharynx.

The second stage is concerned with the passage of the swallowed material through the pharynx. This stage is short in duration, and is a highly complicated and integrated mechanism. In order for the swallowed material to continue on its intended course into the esophagus, it is necessary that other pathways into the pharynx be closed. This is accomplished by a number of almost simultaneous actions.

The swallowed material is prevented from re-entering the mouth by the retracted and elevated tongue against the hard palate and also by the contraction of the posterior pillars of the fauces which tends to close off the cavity of the mouth. Above, the nasopharynx is sealed off by the elevation of the soft palate which comes in contact with the posterior pharyngeal wall. The entrance into the larynx and trachea is effectively closed off by the elevation and forward movement of the larynx, due mainly to the action of the mylohyoid muscles. This results in the larynx coming to rest under the base of the tongue. Both the true and false vocal cords are approximated and this further aids in sealing off the respiratory pathway.

At the completion of the above described events, which requires only a fraction of a second, the pharyngeal constrictors contract to produce a rapid peristaltic wave.[8] This wave arises at about the level of the laryngeal opening and propels the bolus toward the opening of the esophagus. The cricopharyngeus muscle, which has kept the esophagus closed until now, relaxes as the oncoming bolus approaches and allows it to enter the upper esophagus. The peristaltic wave continues into the esophagus to become the primary esophageal peristaltic wave.

The third stage of deglutition involves the passage of liquids and solids through the esophagus. This stage of deglutition varies somewhat with the handling of liquids and a solid bolus. The mechanisms of each will be discussed in detail under esophageal transport.

Types of Esophageal Contractions

In the normal individual, three types of esophageal contractions have been described.

The primary peristaltic contraction, according to Templeton,[8] actually originates in the pharynx during the second stage of deglutition. From the pharynx, this peristaltic contraction travels down into the esophagus in an unbroken manner to the level of the diaphragm. The rate of propa-

gation of the peristaltic wave becomes progressively decreased as it descends the esophagus. The faster rate of travel in the upper esophagus is thought to be due to the striated muscle which is found there.[9] By actual measurement of the time required for the primary peristaltic wave to reach different levels of the esophagus, it has been found that it takes 3.2 seconds for the peak pressure produced by the wave to occur in the upper, 6.3 seconds in the middle, and 9.7 seconds in the lower esophagus.[10] From data such as these, it has been computed that the velocity of a primary peristaltic wave varies from 2 to 3 cm. per second.[6, 10]

The mechanism of production of the primary peristaltic contractions is entirely reflex. The afferent limb of the reflex arc is principally the pharyngeal branches of the glossopharyngeal nerve. The efferent limbs of the reflex arc are the vagi. Central connections of the arc are thought to be in the medulla in the neighborhood of the vagus nucleus. Certain observations indicate that there is considerable central integration responsible for the orderly manner in which the primary peristaltic wave descends down the esophagus. For example, when a primary peristaltic wave approaches a local pathological process, such as an annular carcinoma of the mid-esophagus, interrupting the local muscular and neural elements, the peristaltic wave ceases upon reaching the lesion, only to be observed a moment later appearing below the lesion and continuing on towards the stomach.[8] Local neural connections, the Auerbach plexuses, also may be of importance in the propagation of the primary peristaltic wave.

The secondary peristaltic contraction occurs in the normal esophagus only in response to distention. The distention may be localized such as that produced either by a solid bolus of food or experimentally in response to the distention of a small balloon placed in the esophagus. Kramer and Ingelfinger[11] have determined the average rate of occurrence of secondary contractions induced by a distended balloon, and found it to be 9.5, 6.5, and 8.1 waves per minute in the upper, middle, and lower parts of the esophagus, respectively.

Distention over a considerable portion of the esophagus, as occurs with liquids, also may result in the production of secondary peristaltic waves.[8] When such contractions are observed roentgenoscopically, they usually arise in the region of the arch of the aorta. A segment of the esophagus is seen to undergo spontaneous contraction which forces barium both toward the mouth and stomach. The contraction wave then proceeds to move down the esophagus in a manner similar to the primary peristaltic wave. That the secondary peristaltic wave is definitely propulsive in nature also has been demonstrated by balloon studies.[11]

Tertiary esophageal contractions have been observed and described in apparently normal individuals past middle age. These contractions occur irregularly and locally, and are observed in the lower esophagus. They are not peristaltic. Their function is not known. Tertiary contractions occur rapidly and are of brief duration. Roentgenologically, they may produce a varied picture such as a serated or beaded appearance, multiple

diverticula-like pockets, and sometimes a picture which is referred to as "curling" and the "corkscrew esophagus." It has been suggested that contractions of the spiral muscular coat of the lower esophagus account for this phenomenon.[12] Although Carlson[13] may have observed the tertiary type of contraction using a balloon method to study esophageal motility, tertiary contractions apparently have not been observed using pressure devices. Roentgenologically, they are observed to occur spontaneously. Also, at times, they are seen to appear in the lower esophagus when a primary peristaltic wave has reached about the level of the aortic arch. The peristaltic wave may stop at this level or continue down the esophagus to obliterate the tertiary contractions.

Esophageal Transport

Transport within the esophagus, as in other parts of the alimentary canal, is dependent upon a gradient of pressure to move materials within the lumen. In the esophagus, the principal factor producing this pressure gradient is the primary peristaltic contraction. It has been stated that the peristaltic contraction is preceded by a wave of relaxation.[8, 14] This statement apparently has not been based on experimental evidence but upon the "law of the intestine" proposed many years ago by Bayliss and Starling.[15] They found that mechanical stimulation of the intestine caused contraction above and relaxation below the point stimulated. There is no evidence that the increased pressure produced by the esophageal peristaltic contraction is preceded by a reduction in intraluminal pressure, indicating that relaxation occurs ahead of the peristaltic wave. There are also doubts of the validity of the "law of the intestine" as applied to the intestinal tract. Later investigators[16, 17] have been unable to confirm the observations of Bayliss and Starling. It would seem that the important factor concerned with transport in the esophagus is that some propelling force exists, not whether the canal ahead is relaxed or offers resistance.

In transport of a solid bolus, the primary peristaltic contraction is of particular importance. It sweeps the bolus ahead of it as it progresses from the upper to the lower esophagus. If the primary peristaltic wave is ineffective due to the size, consistency or dryness of the bolus, secondary peristaltic contractions occur which complete the transport of the bolus through the esophagus. These latter contractions, produced by bolus distention of the esophagus, are initiated locally.

The manner in which liquids are transported through the esophagus is dependent upon the position of the subject since gravity apparently plays an important role. In the upright position, liquids may travel through the esophagus at a speed that greatly exceeds the rate or propagation of the primary peristaltic wave. This rapid transfer of liquid to the lower end of the esophagus is considered to be due to the propelling force created by the contraction of the pharyngeal constrictors during the second stage of deglutition, as well as by the action of gravity upon the swallowed liquid. Thus, from an area of positive pressure, the liquid is more or less squirted into the lumen of the esophagus, in which there is a negative pressure. In the upright position, the rapid passage of liquids through

the esophagus requires only a few tenths of a second, and occurs while the esophagus is relaxed and before the primary peristaltic contraction in the esophagus has begun. Fluoroscopy has shown that swallowed liquids are usually arrested at the lower end of the esophagus and await the arrival of the peristaltic contraction before they are admitted into the stomach. At times, however, when a series of swallows occurs rapidly, as when drinking a glass of water, the liquid may pass on through the cardia with little pause and enter the stomach within a second or two after drinking has begun. Almost everyone has experienced this when drinking a very cold or very hot substance by becoming aware of an almost immediate feeling of cold or warmth in the epigastrium. When a quick succession of swallows occurs, the primary peristaltic wave is inhibited until the last swallow is finished. The peristaltic wave then passes down the esophagus emptying any remaining contents.

In either the supine or head down position, the force of gravity is eliminated and the liquid bolus is handled in a manner similar to a solid bolus; i.e., transport is dependent upon the primary peristaltic wave.

The exact mechanism of esophageal evacuation into the stomach has been a matter of much dispute and still has not been established. Lerche[12] has postulated a mechanism of esophageal evacuation which is based on detailed anatomic studies and roentgenographic correlations. His anatomical findings indicated the presence of two dilatations of the lower end of the esophagus as demonstrated in Figure 1.

The upper dilatation is called the esophageal ampulla, and the lower one the gastroesophageal vestibule. The ampulla is simply a bulbar dilatation

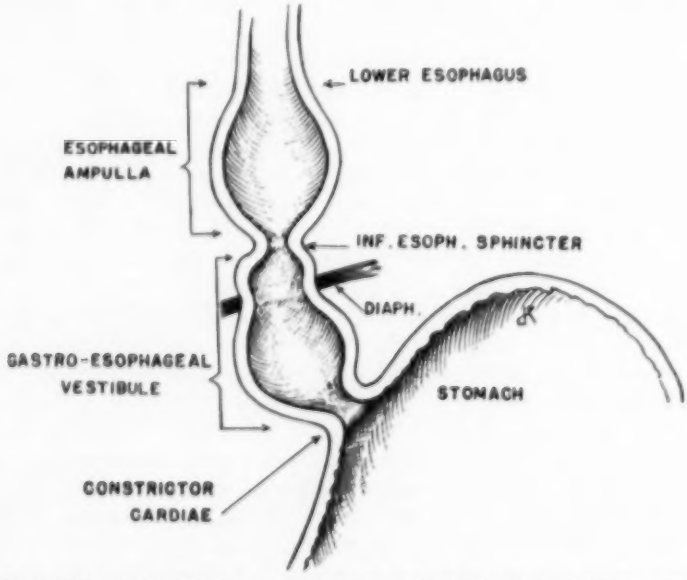

FIGURE 1: Schematic diagram of anatomy of the distal esophagus, according to Lerche.[12]

of the lower end of the esophagus. It is separated from the gastroesophageal vestibule by the "inferior esophageal sphincter." The gastroesophageal vestibule is separated from the stomach by the "constrictor cardiae" which also is said to have a sphincteric action. The intradiaphragmatic portion of the esophagus is the gastroesophageal vestibule, the diaphragm encircling the vestibule at the level of about one centimeter below the inferior esophageal sphincter.

Lerche believes the inferior esophageal sphincter normally remains tonically closed and opens mechanically or reflexly to the peristaltic pressure above the ampulla. After the inferior esophageal sphincter has opened, the ampulla contracts forcing its contents into the vestibule. When the vestibule is filled, being closed below by the constrictor cardiae, the inferior esophageal sphincter contracts. The constrictor cardiae now relaxes and the vestibule contracts and shortens itself, emptying its contents into the stomach. As the vestibule relaxes, it elongates and extends through the open constrictor cardiae, everting a portion of the vestibular mucosa into the stomach.

Esophageal Pressures

With the development of techniques for determining esophageal intraluminal pressures directly, a clearer conception of the mechanical factors involved has been possible. It is desirable to discuss these pressures on the basis of their origin. In the normal esophagus, three types of pressures have been observed. These include: (1) basal pressure, which is the intraluminal pressure of the resting esophagus; (2) respiratory and cardiovascular pressures, which are transmitted to the lumen of the esophagus and are superimposed on basal pressure; and (3) pressures resulting from deglutition or spontaneous esophageal motor activity.

Basal Pressure: Basal intraluminal pressure is defined as that pressure existing within the lumen of the esophagus when there is an absence of

TABLE I: ESOPHAGEAL PRESSURES

Author	Site of Recorder	Origin of Pressure		Mean Pressure
Hightower[5]	Lower Half	Basal		-5.5 cm. H_2O
	Lower Half	Respiration		6.5 cm. H_2O
	Lower Half	Cardiovascular		2.4 cm. H_2O
Butin, et al.[10]	Mid Esophagus	Primary Wave	Liquid	100 cm. H_2O
			Solid	74 cm. H_2O
Hightower[20]	Junction, Mid and Lower Third	Primary Wave	Liquid	88 cm. H_2O
			Solid	72 cm. H_2O
Sanchez, et al.[6]	Upper Seven-Eighths	Primary Wave	Dry and Liquid	40-110 mm. Hg.
Hightower[5]	Mid Esophagus	Secondary Wave	Balloon	32 cm. H_2O
Sanchez, et al.[6]	Ampulla	Primary Wave	Liquid	27 mm. Hg.*
	Vestibule	Primary Wave	Liquid	5-15 mm. Hg.

*One observation only

motor activity. Various factors influence the basal pressure such as the tonus of the muscular wall of the esophagus and intrathoracic and intra-abdominal pressures. Variations in pressure due to respiratory movements and cardiovascular pulsations, and the presence of certain adjacent viscera which may exert a compression or traction upon the esophagus also may influence intraluminal pressure. The most important factor which influences basal pressure is that the esophagus is subjected to the negative pressure that exists within the thoracic cavity.

Basal pressure determined by a direct measuring method,[5] in a group of normal adults, was found to be —5.5 cm. of water when recorded from the middle third of the esophagus. (Table I).

Respiratory and Cardiovascular Pressures: Superimposed upon the negative basal intraluminal pressure are pressure changes due to respiration and cardiovascular pulsations. Inspiration produces a further increase in the negative intraluminal pressure while expiration decreases the negative intraluminal pressure. (Figure 2). Respiratory pressure changes usually vary from 4 to 12 cm. of water pressure. In normal adults, eupnic respiration was found to produce a mean pressure change of 6.5 cm. of water when recorded from the lower esophagus.[5] (Table I).

Changes in esophageal intraluminal pressure due to cardiovascular pulsations are usually quite constant in any one individual, but have been found to vary from 1.2 to 3.6 cm. of water in different individuals. When recorded from the lower esophagus, the mean pressure change which cardiovascular pulsations produced was 2.4 cm. of water.[5] Both respiration and cardiovascular pulsations produce a greater change in intra-

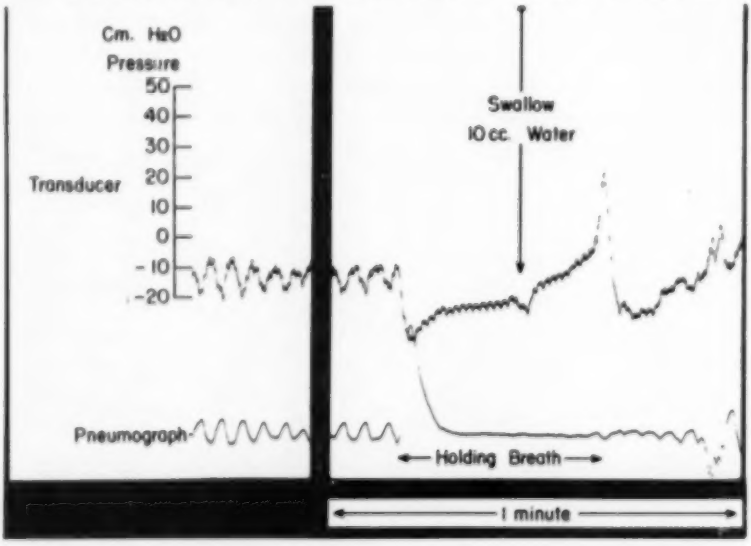

FIGURE 2: Example of deglutition pressure pattern recorded from mid esophagus illustrating the initial negative wave and subsequent positive waves of pressure. Note the entire complex occurred while respirations were voluntarily inhibited. (From Hightower, N. C., Jr.[5])

luminal pressure in the esophagus than in any other site within the alimentary canal.

Deglutition Pressures: Characteristic pressure changes occur within the esophagus during the act of swallowing. Butin and associates,[10] using a method of recording esophageal intraluminal pressures directly,[5] have made an extensive study of pressure changes occurring within the esophagus of normal individuals following deglutition. They had their subjects swallow liquid as well as a solid bolus; and recorded the pressure changes in the upper, middle, and lower esophagus. In these studies, they found a characteristic pattern of pressure change regardless of whether the subject swallowed liquid or a solid bolus. They termed this pattern, which consisted of an initial negative wave followed by three positive waves, the "normal swallowing complex."

The initial negative wave in the "normal swallowing complex" described by Butin and associates was observed 42 years ago by Schreiber,[18] using a balloon technique to study esophageal motility. Schreiber and later Lerche attributed the initial negative wave as being due to the stretching of the esophagus resulting from the elevation of the larynx. During the second stage of deglutition when elevation of the larynx occurs, the esophagus is closed off at both the pharyngeal and cardiac ends. With the elevation of the larynx, the esophagus is pulled up in front by the tendon of its longitudinal muscle layer and in back by the stylo-pharyngo-palatino-esophageal muscle apparatus.[12] As both ends of the esophagus are closed, this elongation results in the negative intraluminal pressure already present becoming more negative. In the studies of Butin, et al., the initial negative wave was observed in about a third of the complexes recorded from normal individuals. It occurred more frequently in the upper and lower third of the esophagus than in the middle third. If the mechanism of production of this negative wave is as postulated by Schreiber and Lerche, one might expect to observe it more frequently in the upper and lower esophagus as contrasted to the middle portion. It is at the ends that the esophagus is anchored, and a pull or stretch of the organ might produce a greater negative pressure in these areas than in the mid-portion. Butin et al. found the initial negative wave to occur immediately after the onset of swallowing, that is, usually within 0.1 second, and that it was approximately 0.4 seconds in duration, and the mean negative pressure produced was 8.4 cm. of water.

Sanchez, Kramer, and Ingelfinger,[6] using open tipped catheters to record esophageal deglutition pressures, stated they rarely observed the initial negative pressure wave described above. They attributed minor significance to the wave as a component of the normal pressure complex. Ingelfinger[19] questions whether the initial negative wave is an essential feature of the swallowing complex or whether or not it is related to the respiratory phase and fixation of the diaphragm at the onset of swallowing. That the initial negative wave is an integral part of the esophageal deglutition pressure pattern and not related to respiration is evident from Figure 2. This illustration clearly shows the initial negative wave in a deglutition

pressure pattern recorded while the subject held his breath. Butin et al. have adopted the explanation offered by Schreiber and Lerche for the mechanism of production of the initial negative wave and the available data indicate that such an explanation is correct.

The second component of the "normal swallowing complex" is an abrupt and almost instantaneous positive pressure change. This sudden increase in pressure is shown in Figure 2 where it is seen to occur immediately after the negative pressure wave. Sanchez et al. attribute this component of the pressure complex to the sudden injection of liquid into the esophagus as they observed it to occur simultaneously in the upper seven-eighths of the esophagus after swallowing liquids. It was seldom observed after a "dry" swallow.

Butin and associates favor the explanation that the origin of the sudden pressure change is due to transmission of buccopharyngeal pressures into the esophagus. The exact origin of this component of the pressure pattern has not been determined. It was observed in 87 per cent of the records studied by Butin, et al. They found that the time of onset of the first positive wave varied with the depth of the transducer in the esophagus, beginning at 0.5, 0.8, and 1.5 seconds in the upper, middle, and lower parts of the esophagus, respectively. The magnitude of the first positive pressure wave is usually about 12 cm. of water.

Following the abrupt positive pressure wave just described, the third component of the pressure complex occurs. This consists of a slowly increasing positive pressure change, or else a plateau of positive pressure is maintained. Rarely, after the first positive pressure wave does there occur a decrease in pressure. The origin of this component of the pressure pattern is thought to be related to the approaching peristaltic wave and to represent a slowly increasing pressure head. The time of onset and duration of this second positive pressure wave increases as the recording device is placed deeper into the esophagus. These time relationships strongly suggest that this component of the pressure pattern is related to the primary peristaltic contraction. Butin, et al. give the time of onset as 1.5, 2.7, and 4.4 seconds in the upper, middle, and lower parts of the esophagus. The greatest pressure attained, found in the lower esophagus, was 21.9 cm. of water. Sanchez, et al. state the duration of this component of the pressure pattern varies from two to 19 seconds.

The fourth and most prominent component of the deglutition pressure pattern is a large, simple, monophasic, positive pressure wave which rises rapidly to a peak pressure and declines with equal speed. It immediately follows the gradual rise or the plateau of pressure described above. This wave, which has been described in detail,[6, 10] represents the pressure produced by the primary peristaltic wave. Butin and associates found that mean values for the time elapsed from swallowing to the beginning of the wave were 2.1 seconds in the upper, 5.1 seconds in the middle, and 7.9 seconds in the lower esophagus. They noted that the peak pressure occurred at 3.2, 6.3, and 9.7 seconds in the upper, middle, and lower esophagus, respectively. When recorded from the middle esophagus with the

subject in the supine position, it was found that a 15 ml. swallow of water produced a mean peak pressure of 100 cm. of water while a solid bolus produced a pressure of 74 cm. of water. (Table I). A later study, using the same method of recording pressures, gave similar results.[20] In this study, subjects were given 10 ml. of water to swallow and the pressure transducer was located at the junction of the middle and lower third of the esophagus. The liquid produced a peak pressure of 88 cm. of water and with a solid bolus (2 by 1 cm. circular piece of white bread) a pressure of 72 cm. of water was recorded (Table I). In still another study using open-tipped catheters filled with water and connected to Sanborn electromanometers, Sanchez, Kramer, and Ingelfinger[6] found the peak pressure from swallowing liquids to vary from 40 to 110 mm. Hg. in the upper seven-eighths of the esophagus (Table 1). The duration of the pressure wave produced by the primary peristaltic contractions varies from 2.3 seconds in the upper to 3.0 seconds in the lower esophagus.[10]

Secondary Peristaltic Pressures: With the methods employed to register deglutition pressures, as given above, distention of the esophagus is not produced, and secondary peristaltic waves and their accompanying pressure changes are rarely observed. By distending the esophagus with a small (35 ml. capacity) water-filled balloon under 15 cm. of water pressure and recording simultaneously with a pressure transducer, secondary peristaltic contractions can be induced and the pressure changes resulting from such contractions have been recorded.[5] The secondary peristaltic contraction produces a pressure wave similar to the final pressure wave of the deglutition pressure pattern. It is a simple, monophasic, positive pressure wave which arises rapidly to a peak then returns promptly to the base line. An analysis of 54 secondary peristaltic pressure waves recorded from the mid esophagus revealed the mean peak pressure waves attained to be 32 cm. of water (Table I). The mean duration of the waves was 7.6 seconds. The secondary peristaltic contractions were observed to occur spontaneously at a rate of 4 to 6 per minute.

Pressure Changes in the Distal Esophagus: A recent investigation of pressure changes in the distal esophagus during deglutition has been carried out by Sanchez, Kramer, and Ingelfinger.[6] The authors have adopted the anatomical terminology proposed by Lerche in reporting their findings. In the esophageal ampulla, they recorded a pressure pattern following deglutition which was similar to that observed in the lower esophagus but different in some important respects. The initial positive pressure wave was present and this was followed by a plateau of pressure. The positive pressure wave due to the primary peristaltic contraction was observed to rise rapidly to a peak; but, instead of dropping off rapidly, it returned to the base line in a gradual slope with respiratory pressure changes superimposed upon the slowly declining wave. The peristaltic pressure wave in the ampullary complex had a duration of 15 to 22 seconds and traveled at a rate of 0.7 to 1.2 cm. per second. The average height of the wave is not given, but one published record indicates that it is approximately 27 mm. Hg. (Table 1). The authors point out that the

characteristics of the ampullary deglutition pressure pattern are compatible with fluoroscopic observations which show that the peristaltic wave slows down as it reaches the lower esophagus. As characteristic ampullary complexes were recorded from a patient with a large diaphragmatic hernia and also one with paralysis of the left diaphragm, it would seem that the diaphragm is unimportant in the production of the pressure pattern. There is little doubt that the pressure pattern represents esophageal peristalsis.

From the vestibule, a decidedly different pressure pattern was observed. Records from this area showed only a gradual rise and fall of pressure lasting from 20 to 40 seconds. There was an absence of the first positive pressure wave. The maximum pressure attained was only 5 to 15 mm. Hg. (Table I). These observations indicate that the vestibule is not in communication with the lower esophagus but is closed off, possibly as suggested by Lerche by the inferior esophageal sphincter. This is in keeping with the fluoroscopic observation that liquids frequently collect in the lower esophagus above the diaphragm and await the arrival of a peristaltic wave before being emptied into the stomach. If the gastroesophageal vestibule exists as a separate anatomical entity, one must postulate a separate motor activity—one that is highly integrated with the motor activity of the lower esophagus. These pressure observations in the distal esophagus seem to support the mechanism of esophageal evacuation proposed by Lerche. They would not support the mechanism of esophageal emptying proposed by Mosher in which the diaphragm supposedly takes an active part.[21]

Disturbances of Deglutition by Disease

The term dysphagia means difficulty in swallowing. As it applies to the entire act, a disturbance in one or more of the stages of deglutition may give rise to dysphagia. Dysphagia is only a symptom, and it is not pathognomonic of any one specific disease. Pain may or may not be asso-

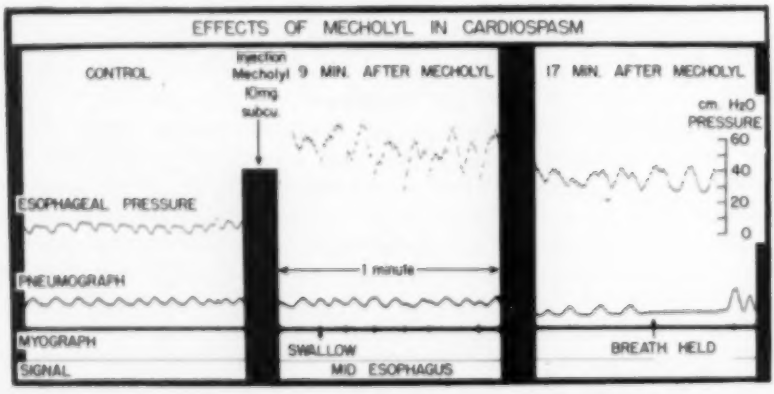

FIGURE 3: Effects of Mecholyl on esophageal intraluminal pressure in cardiospasm. Note the marked rise in intraluminal pressure at 9 and 17 minutes after subcutaneous administration of 10 mg. of Mecholyl. (From Hightower, N. C., Jr., Olsen, A. M. and Moersch, H. J.[20] Reproduced with kind permission of the editor of *Gastroenterology*.)

ciated. The occurrence of dysphagia may indicate serious disease, therefore, its presence usually warrants thorough clinical investigation, including roentgenoscopic and endoscopic examination of the esophagus.

Dysphagia due to emotional and psychic disturbances, as well as the psychosomatic aspects of cardiospasm, are purposely omitted.

Dysphagia of the First and Second Stages of Deglutition: There are many causes of dysphagia resulting from disturbances of the first and second stages of deglutition. Only a few will be mentioned.

Any painful inflammatory process involving the mouth, tongue, or pharynx may make swallowing difficult. Neoplasms of the tongue or posterior pharyngeal wall can interfere with the passage of a bolus into and through the pharynx. Pharyngeal paralysis is a common cause of dysphagia involving the second stage of deglutition. In such instances, it may be impossible for the soft palate to be elevated, thus, allowing liquids to be regurgitated through the nose. The pharyngeal constrictors may be unable to initiate the peristaltic contraction which empties the contents of the pharynx into the esophagus. Pharyngeal paralysis usually results from a bulbar lesion as seen in syringomyelia, poliomyelitis, cerebrovascular hemorrhage, and multiple sclerosis. Cranial nerve (glossopharyngeal) neuritis also may result in pharyngeal paralysis. Myasthenia gravis can produce dysphagia by interfering with the second stage of deglutition. Diphtheria is sometimes followed by palatine and pharyngeal paralysis which produces dysphagia.

Mobility of the larynx is essential to the second stage of deglutition, and any disease process which prevents the larynx from ascending to lie beneath the base of the tongue causes marked dysphagia. Neoplasms, such as carcinoma of the larynx and thyroid, and infectious processes, such as tuberculosis and syphilis, may result in fixation of the larynx; thus, making swallowing extremely difficult. A few congenital anomalies, such as cleft palate, may also produce dysphagia.

Dysphagia of the Third Stage of Deglutition: Any interference with transport through the esophagus may cause dysphagia. The process may be inflammatory, as in esophagitis; obstructive, as occurs with carcinoma or benign stricture; neurogenic, as in cardiospasm or possibly diffuse spasm; or due to some systemic disease such a generalized scleroderma.

Cardiospasm: The etiology and mechanism of lower esophageal obstruction in achalasia or cardiospasm has been a matter of much dispute. The consensus of opinion today holds that cardiospasm is not a localized process which produces "spasm of the cardia" but one in which most, if not all, of the esophagus is involved.[1, 2, 3, 19, 22] This idea was suggested by Hurst[23] when he recommended the term achalasia instead of cardiospasm. It was Hurst's opinion that achalasia was due to a degeneration of the myenteric plexus of the esophagus and not to hypertrophy and spasm of the cardiac sphincter. More recent investigations into the pathologic changes of cardiospasm have revealed a marked degeneration of Auerbach's plexus, especially in the lower parts of the esophagus.[24, 25, 26, 27] The unusual sensitivity of the cardiospastic esophagus to Mecholyl (Figure 3)

supports the pathologic findings that achalasia is due to a disorder of the intrinsic nerve plexuses.[2, 3, 20, 28] The effect of Mecholyl is in keeping with Cannon's law of denervation.[29] This drug produces a marked contraction of the dilated atonic esophagus. (Figure 4).

The disturbance of motility which occurs in cardiospasm also indicates that the condition is not one of simple obstruction at the cardia. Motor activity of the esophagus in cardiospasm has been studied by roentgenologic,[22, 30] balloon-kymographic,[2, 3] and pressure detecting techniques.[6, 10, 20]

In a study of 39 patients with cardiospasm, Templeton[22] found at fluoroscopy that in all but three the primary peristaltic wave traveled only to about the level of the suprasternal notch or the superior margin of the aortic arch. In one of the patients, the primary wave did not go beyond the level of the cricopharyngeal muscle. In two patients, the primary wave continued on down the esophagus, but its depth was insufficient to influence the passage of the bolus. No secondary peristaltic waves were observed. In all but two of these patients, Templeton noted "purposeless, shallow, segmented contractions constantly appeared and disappeared at different levels of the esophagus." This type of motor activity was most prominent in patients with only slight dilatation. These contractions were similar to the tertiary contractions he observed in normal individuals. In addition to these undulating waves, generalized tonic contractions were observed which would force barium into the stomach when they produced a diffuse narrowing of the esophageal lumen. Wolf and Almy,[30] in a fluoroscopic study of 14 patients with cardiospasm, also noted the undulating contractions of the lower esophagus described by Templeton. In addition, they found that in nine of the 14 patients a

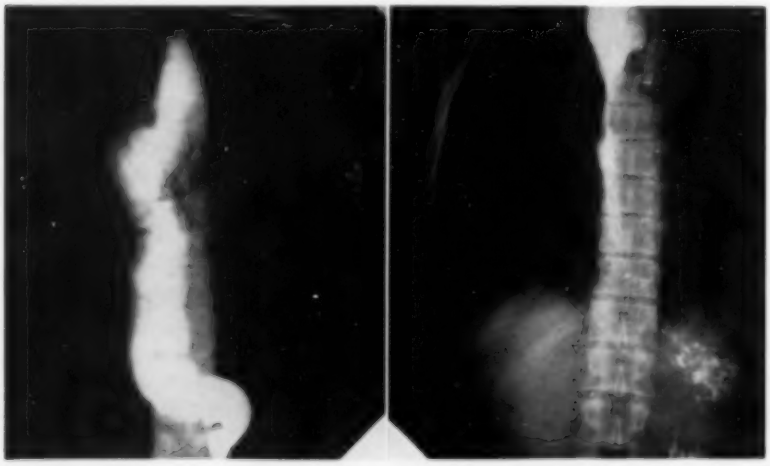

FIGURE 4A FIGURE 4B

FIGURE 4: Esophagus in a patient with cardiospasm before and after administration of Mecholyl: *A*. Marked dilatation and tortuosity of the esophagus; *B*. Changes noted 9 minutes after subcutaneous administration of 10 mg. of Mecholyl. (From Hightower, N. C., Jr., Olsen, A. M. and Moersch, H. J.[20] Reproduced with kind permission of the editor of *Gastroenterology*.)

sustained contraction of the diaphragm would intensify the degree of esophageal obstruction.

Abnormal motor activity in cardiospasm also has been demonstrated by balloon methods. Kramer and Ingelfinger[2] have found decreased tone, lack of propulsion, and irregular phasic activity in the lower two-thirds of the esophagus. These findings have been confirmed by Sleisenger, Steinberg, and Almy.[3]

Butin, Olsen, Moersch, and Code[10] have compared esophageal intraluminal pressures in normal individuals and in patients with cardiospasm, and have found some important differences. Spontaneous motility was observed frequently (18.5 per cent) in the records obtained from patients with cardiospasm. In one, the incidence of spontaneous motility was reduced from 44 to 18.5 per cent by therapeutic dilatation which relieved most of his dysphagia. In another study,[20] using the same technique of recording pressure, spontaneous activity was rarely observed following careful aspiration of the esophagus. This suggests that spontaneous activity is related to the degree of obstruction and retained secretions or swallowed material.

From an analysis of records, obtained, after deglutition, from patients with cardiospasm, Butin and associates found there was no fixed pattern of waves of pressure. Most of the pressure responses, however, were of three types: complexes that resembled the normal swallowing complex; absence of pressure waves related to deglutition; and multiple phasic contractions in response to a single swallow. An example of the abnormal

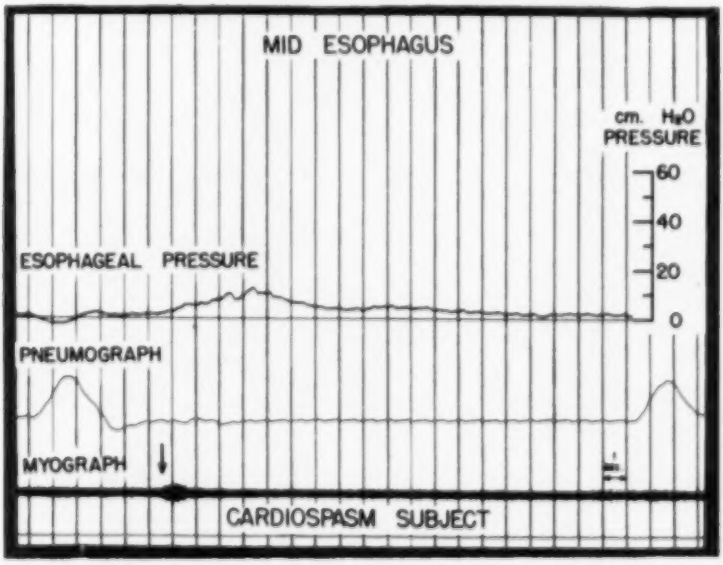

FIGURE 5: Deglutition pressure pattern recorded from mid esophagus of patient with cardiospasm. Note complex was recorded during breath holding and consists of only slight, irregular positive pressure wave. (Published through courtesy of Dr. C. F. Code, Section on Physiology, Mayo Foundation.)

pressure pattern observed in cardiospasm following deglutition is seen in Figure 5.

In a comparison of deglutition pressures in normal persons and patients with cardiospasm, it was found that a 10 ml. swallow of water produced a mean peak pressure of 87.9 cm. of water in normals and only 24.8 cm. of water in patients with cardiospasm. A solid bolus resulted in a peak pressure of 71.6 cm. of water in the normals and 17.3 cm. of water in those with cardiospasm.[30]

Diffuse Spasm: Moersch and Camp,[31] in 1934, first described diffuse spasm of the lower part of the esophagus as a clinical entity. Dysphagia due to diffuse spasm usually is intermittent and painful. Roentgenoscopically, three types of disturbed motor activity have been described: (1) diffuse, irregular spasm of the lower half or third of the esophagus; (2) diffuse narrowing of the lower half or third of the esophagus, suggesting tetanic spasm; and (3) multiple spastic segments of concentric narrowing. Characteristic of diffuse spasm is an absence of marked dilatation above

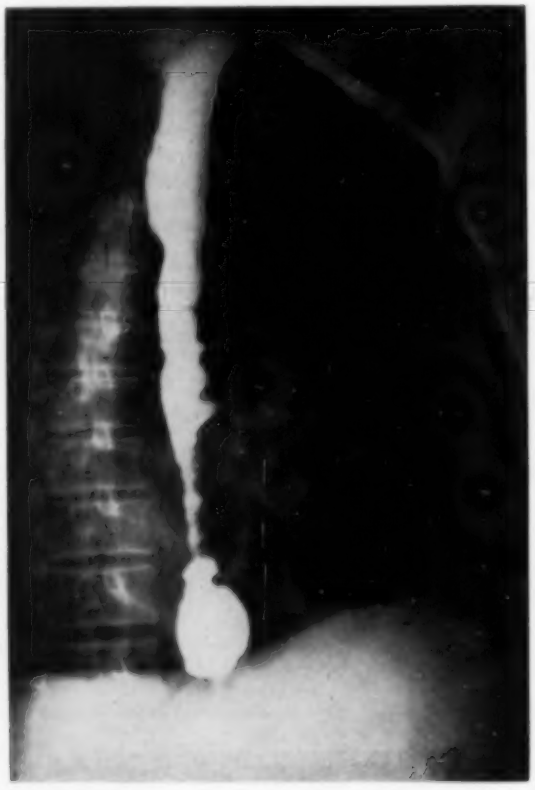

FIGURE 6: Roentgenographic picture of diffuse spasm of lower esophagus. Note irregularity of contraction producing pseudodiverticula and minimal dilatation proximal to point of obstruction.

the area of constriction. (Figure 6). The etiology of diffuse spasm has not been established, but it is thought that the localized intermittent spasm is reflex in origin as it is frequently associated with upper gastrointestinal disease.

Few observations of esophageal motility, other than roentgenoscopic descriptions, have been made in diffuse spasm. Recently, however, esophageal pressures in two patients with diffuse spasm were studied.[20] It was found that a 10 ml. swallow of water produced a mean peak pressure of 52.3 cm. of water, while a solid bolus resulted in a peak pressure of 47.7 cm. of water. Unlike cardiospasm, Mecholyl does not produce a significant increase in intraluminal pressure in patients with diffuse spasm.

Mechanical Obstructions: Dysphagia produced by mechanical obstruction of the esophagus may be caused by intrinsic or extrinsic lesions. Intrinsic lesions include congenital anomalies as stenosis and bands; inflammatory processes, as esophagitis due to peptic ulceration, or swallowed caustics which may result in stricture; neoplasms, as carcinoma (Figure 7) and benign tumor; and foreign bodies. Examples of extrinsic lesions which produce mechanical obstructions are large inflammatory periesophageal lymph nodes, lymphomas, and aneurysms.

In general, most conditions causing mechanical obstruction of the esophagus produce similar disturbances in motility. When a small incomplete obstructive lesion involves the upper or middle esophagus, the primary peristaltic contraction may be observed fluoroscopically to "skip over" the lesion. When the obstruction exists in the lower esophagus, the primary peristaltic wave usually progresses to the site of the lesion with-

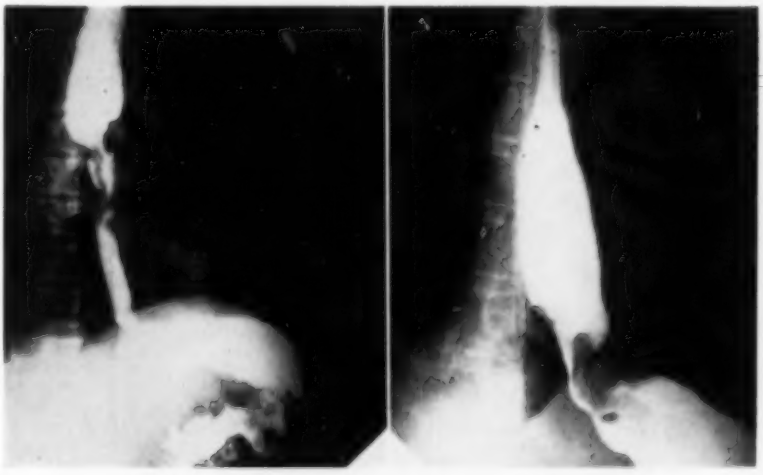

FIGURE 7A FIGURE 7B

FIGURE 7: Illustrations of carcinoma of the lower esophagus: *A*. Constricting carcinoma of junction of middle and lower third of esophagus. Note moderate dilatation proximal to obstruction. History of dysphagia for three months. *B*. Obstructing carcinoma of distal esophagus with extension into cardia of stomach. Marked dilatation proximal to obstruction. Dysphagia with pain had been present for one year.

out interruption. In some instances, the waves will be shallow and not strong enough to force the barium past the stenosed portion.[22] As most obstructive lesions occur in the lower esophagus, distention of the proximal esophagus with retention of secretions and swallowed material is not unusual. The distention acts as a stimulus for secondary peristaltic contractions, and these waves frequently are observed at the time of roentgenologic examination.

Using a balloon-kymographic method, investigations of motility in two patients with mechanical obstruction of the lower esophagus revealed decreased esophageal tone and a wave pattern consisting of strong, rhythmical contractions occurring at a rate of 4 to 6 per minute. In each patient, the inflated balloon was carried down to the point of obstruction before its progress was arrested.[11] There is little doubt that the wave pattern described represented secondary peristaltic contractions.

Deglutition pressures have been determined in one patient with a benign stricture of the distal esophagus. Swallows of 10 ml. of water produced

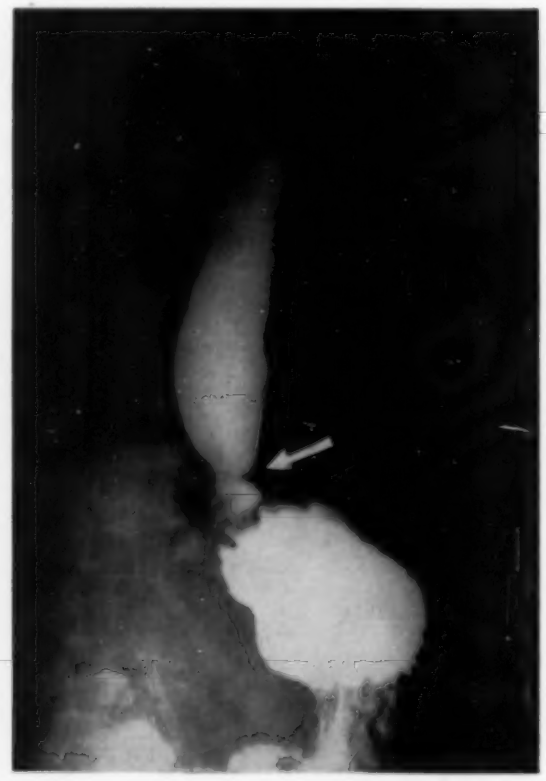

FIGURE 8: Scleroderma involving the esophagus. Cutaneous scleroderma present 4 to 5 years, the dysphagia for 16 months. Note constriction of distal esophagus just above "phrenic ampulla" with atony and dilatation of the lower esophagus. Minimal obstruction to barium flowing into stomach in upright position.

a mean peak pressure of 66.7 cm. of water at the junction of the middle and lower third of the esophagus. A solid bolus resulted in a mean peak pressure of 34.2 cm. of water. Although these pressures are not as great as those recorded from normal individuals, they exceed the deglutition pressures observed in cardiospasm, diffuse spasm, and scleroderma. In mechanical obstruction of the esophagus, Mecholyl does not produce the marked increase in intraluminal pressure as observed in cardiospasm.[20]

Scleroderma: Like cardiospasm, scleroderma apparently involves most, if not all, of the esophagus. Lindsay, Templeton, and Rothman[32] studied five patients with scleroderma roentgenoscopically, and found that the primary peristaltic contraction in four progressed only to the level of the suprasternal notch and ceased entirely. In one of the patients the contraction continued on down the esophagus, but was too shallow to push the bolus along. The contraction differed from a normal peristaltic wave in that the esophagus behind the advancing wave did not remain contracted, but distended immediately. Small, ineffective, secondary peristaltic contractions were observed in only one of the patients. In three, a localized narrowing of the esophagus was observed immediately above the "phrenic ampulla." Proximal to this area, mild dilatation was present. An example of the roentgenographic changes seen in scleroderma is illustrated in Figure 8.

In the upright position, swallowed barium passed from the pharynx to the stomach, with some delay at the site of stricture but not at the cardia. In either the supine or Trendelenburg position there was an absence of esophageal transport, the esophagus becoming progressively distended by successive swallows. When the esophagus filled, each swallow then forced small amounts of barium into the stomach, apparently, by transmitting pressure through the column of barium. The esophagus was unable to empty itself in the horizontal position, but if the patient was raised to a sitting or standing position, most of the barium passed into the stomach.

In balloon-kymographic studies of the disturbed motility in four patients with scleroderma, Kramer and Ingelfinger[11] have reported a marked decrease in esophageal tone. They noted that propulsion of the inflated balloon down the esophagus was slow or absent. The wave pattern recorded by the balloon from the upper, middle, and lower esophagus was markedly diminished or absent.

Deglutition pressures have been measured in only one patient with scleroderma. In this one it was observed that few primary peristaltic contractions reached the lower esophagus, and those that did were of low amplitude. After swallows of 10 ml. of water, a mean peak pressure of only 10.6 cm. of water was produced, while swallows of a solid bolus resulted in a mean maximum pressure of 11.2 cm. of water.[20]

Mecholyl does not increase esophageal intraluminal pressure markedly in patients with scleroderma.[2, 20]

All of these investigations demonstrate that the primary disorder of esophageal motility in scleroderma is the defective propagation of the

primary peristaltic contraction. As there is little gradient of pressure, transport is definitely retarded. The apparent relaxation demonstrated probably represents myogenic failure.

CONCLUSION

Recent investigations of esophageal motility in health and disease have been reviewed. Although the methods of investigation have varied widely, there is a striking similarity in the results obtained. The data complement one another and their correlation affords a better understanding of the anatomy and physiology of the esophagus in the normal and diseased state. It is not to be implied that all problems have been solved with finality; on the contrary, many avenues of research are now opening. It is to be expected that further investigations along these lines and, in particular, studies of intraluminal pressures will continue to add to our knowledge.

RESUMEN

Se revisaron las investigaciones recientes sobre la motilidad del esófago normal y patológico. Aunque los métodos empleados son muy diferentes los resultados obtenidos son notablemente similares.

Los datos suministrados se complementan entre sí y su correlación permite una mejor comprensión de la anatomía y de la fisiología del esófago normal y patológico. No por éso debe pensarse que todos los problemas han llegado a su solución final. Por el contrario se están abriendo nuevos caminos a la investigación. Es de esperarse que las investigaciones ulteriores en estos lineas y en especial el estudio de la presión intraluminar esophageal agregue más a nuestros conocimientos.

RESUME

L'auteur a passé en revue les investigations récentes concernant la motilité oesophagienne, normale et pathologique. Bien que les procédés d'investigations aient largement varié, il y a une similitude frappante entre les résultats obtenus. Les constatations se complètent l'une l'autre, et leur corrélation permet une meilleure compréhension de l'anatomie et de la physiologie de l'oesophage normal et pathologique. On ne doit pas en déduire que tous les problèmes ont été résolus. Au contraire, beaucoup de voies sont maintenant ouvertes à la recherche. On doit s'attendre à ce que des investigations ultérieures dans cette direction, en particulier l'étude des pressions intra-oesophagiennes, continuent à enrichir nos connaissances.

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The Significance of Small Epidemics of Tuberculosis

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Introduction

Although the title of this talk sounds very different from that of Dr. Tucker as given in the program, nevertheless, what I have to say is pertinent to the main purpose of our organizational existence, namely the control of tuberculosis.

Emil von Behring (1854-1917), Professor of Hygiene at Halle (1894) and Marburg (1895), who has to his credit diphtheria antitoxin, was quite wrong about some other things. In 1903 he asserted that tuberculosis was acquired by infection through the alimentary tract from the ingestion of milk contaminated with bovine tubercle bacilli and that these bovine bacilli were changed in the body of man into the human type. Although he was wrong about the transformation of the bovine bacillus into the human type, he was of course right about the menace of milk from tuberculous cows. He thought also that consumption in the adult was practically always a recrudescence of tuberculous infection acquired in infancy. It was another verse of the song "first muttered in the cradle!" Now, without doubt, tuberculosis acquired during our early years may relapse many years later but it is my thought and it is the theme of my remarks today that much clinical tuberculosis first appears within the first year or two after primary infection and our efforts at control should be directed primarily at this stage of infection. The small epidemics which I have gathered from here and there support this idea.

Childhood Tuberculosis

Arvid Wallgren, a distinguished Swedish pediatrician, in his *time-table of tuberculosis has pointed out* (1948) that in children the first symptoms of meningitis appeared in one to four months after infection in 87.5 per cent of 64 cases; the first symptoms of pleural effusion appeared in one to seven months after infection in 77 per cent of 108 cases; the first symptoms of bone and joint tuberculosis in less than two years after infection in 85 per cent of 106 cases; and finally the first symptoms of pulmonary tuberculosis in less than two years in 78 per cent of 105 cases. I should like to emphasize here not only the sequence of the appearance of specific manifestations of clinical tuberculous disease, first miliary tuberculosis and meningitis, then pleural effusion, then skeletal tuberculosis and then post-primary pulmonary tuberculosis, but also the equally important fact that tuberculous disease in some form followed fairly closely on primary infection. This does not mean that every person infected in childhood will inevitably develop one or the other of the

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mentioned forms of tuberculosis. Without doubt the chances of developing active clinical tuberculosis soon after infection vary with age. The hazard is greatest in infancy and early childhood, less during the ages 7 to 13, increases again during adolescence and young adult life. If the recent converter escapes early, the risk of active disease after a long latent period is still ever present. Chemotherapy for the recent converter with or without symptoms and/or radiological signs may then serve two important purposes. It may prevent the development of disease soon after infection and it may reduce the chance of remote development of clinical disease. The small epidemics here summarized show that active tuberculosis may follow shortly after infection in adult life as well as in childhood.

Epidemic of Tuberculosis in the Faroe Islands

These small islands in the North Atlantic Ocean between Iceland and the Shetlands with a population of about 30,000 people belong to Denmark. Bovine tuberculosis has been eradicated and half the population are tuberculin negative. From time to time small epidemics of tuberculosis have appeared in the Islands and are of great interest since local conditions and public health regulations make it possible to trace the source of infection. One of these epidemics was reported by Axel Poulsen in 1947. A maid servant 20 years old was employed at a certain hotel in the Islands from June 1 to November 2, 1945, when she left for home since she had been feeling ill with cough and expectoration for about one month. She stayed at home from November 2 to November 12, when she was hospitalized and tubercle bacilli were now found in her sputum. On November 28, after only 16 days in this hospital, she was transferred to a sanatorium. This person became the source of two small epidemics of tuberculosis, the first, Group I, among the guests and other employees of the hotel where she had worked and the second, Group II, among the staff of the hospital where she was sent for diagnosis and tuberculosis was discovered.

Discussion of Group I

Since another case of tuberculosis had been discovered in the hotel on October 27, 1945, all the staff and guests had been given tuberculin tests on November 1, 1945. The examination covered 27 persons, of whom 26 had been living in the hotel from three months to five years while one had stayed there only one night. Positive reactions were found in 12 persons and negative in 14 persons. Interest therefore centered on the 13 primarily negative persons who later converted to positive. Five of these 13 came down with pleurisy with effusion and fever, five others showed either fever or radiologic changes, three had no manifest signs of symptoms of infection, other than the conversion of the tuberculin test to positive.

Discussion of Group II

After the patient had been admitted to the hospital and tubercle bacilli found in her sputum, she was transferred to a sanatorium and all her

contacts in the hospital studied. Of the nine converters among her hospital contacts, three developed pleurisy with effusion, two others meningitis and four radiologic changes characteristic of primary tuberculous infection.

Summary

This is a report of a small epidemic involving 22 persons, all of whom were infected by a girl with active pulmonary tuberculosis. Out of these 22 patients, three died of meningitis, seven developed pleurisy with effusion, and eight others were ill for shorter or longer periods with signs and symptoms of primary tuberculosis.

Comment

An x-ray film of the chest on her admission to the hospital would have led to more prompt diagnosis and proper precautions to protect her contacts from infection. This case illustrates not only the hazard of unrecognized tuberculosis in a hospital but the rapidity with which clinical tuberculosis may follow first infection. It also emphasizes the importance of the tuberculin test in the prompt recognition of recent infection.

Small epidemics of tuberculous nature were formerly of frequent occurrence on board the fishing boats which about June first sailed from the Faroe Islands to fish off the West Coast of Greenland and returned about October. If a crew unfortunately included an open case of tuberculosis, the ship might return with hardly any fish because many of the crew were ill and the others had to care for them and the ship and had no time for fishing. Many of these patients had pleurisy or meningitis or other signs and symptoms of primary tuberculous infection. According to Axel Poulsen, these fishing boat epidemics disappeared after enactment in 1939 of a law compelling examination for tuberculosis of the crews of fishing boats setting out from the Faroe Islands.

A Small Epidemic of Tuberculosis on a British Vessel

This epidemic has been reported by W. D. W. Brooks. Toward the end of 1942, a British frigate on prolonged convoy duty mainly in the North Atlantic, returned to Liverpool with three cases of active pulmonary tuberculosis. This led to examination, including x-ray films, of the whole ship's complement of 182 men. Evidence of tuberculosis was found in 20 other members of the crew. Of these 23 persons, active disease was found in 13, unstable and not certainly active lesions in seven and arrested disease in three. It was the opinion of Brooks that at least six of these cases were examples of recent primary infection with continuous spread to adult type disease. Two of the cases were pleurisy with effusion, one of which was quite silent clinically. The source of infection for the recent infections was "most probably" one of the officers, aged 48 with chronic cavitary tuberculosis of the lungs. According to Brooks, since the whole Navy is now x-rayed annually, a small epidemic like this could not occur again.

Black Lady's Epidemic

This is the story of a cow called Black Lady, beautiful animal outwardly but sad to say a victim of tuberculosis. Despite the evidence of a positive tuberculin test she was retained on a farm with the following tragic results. Of the farmer's seven children, five developed clinical tuberculosis from drinking this animal's milk, the oldest, 14 years of age escaped because she did not like and therefore did not drink cow's milk. The youngest also escaped because she was taking mother's milk. One child aged five years got tuberculosis of the spine and a para-vertebral abscess, the four other children had symptoms and radiologic signs of primary tuberculous infection. Four cats and one pig, all fed on Black Lady's milk were slaughtered and found to have generalized tuberculosis. Another cow, stable mate of Black Lady, not fed on milk, was slaughtered and proved to have tuberculosis. Black Lady herself was slaughtered and found to have generalized tuberculosis involving lungs, liver, lymph nodes and udder.

This, then was a small epidemic of tuberculosis among human and other domestic animals due to bovine tubercle bacilli and traceable to one apparently healthy cow. This epidemic was due to man's neglect of the significance of a positive tuberculin test in a cow.

J. Arthur Myers and associates have magnificently applied some of the techniques of governmental eradication of bovine tuberculosis, to the control of tuberculosis in human beings. Neither in the British Isles nor in America do we make the best use of the tuberculin test. In Scandinavia they are way ahead of us, at least in the use of this test to discover spreaders of disease, as the next story of an epidemic in Norway will reveal. I do not underestimate this use, *this public health use of the tuberculin test*, but I shall repeat over and over again that the tuberculin test has tremendous value in the discovery of the recent converter who must be treated promptly with chemotherapy!

Aksel Taering's Exploits or the story of the passage of a carrier of tuberculosis through two small towns in Norway as told by O. M. Andreaes. The author gives an account of an epidemic of tuberculosis which in 1943 hit the little town of Hoyanger in Norway. The source of the infection was a far-advanced tuberculous travelling juggler, a member of a carnival troupe, who during one month's stay in the place infected 54 persons. His guilt was further confirmed by the high incidence of tuberculous infection which followed his visit to another town. The following year two of the first victims "turned bacillary" and infected their families. An infected member of one of these families during military service "turned bacillary" and infected a number of his military companions.

Of the 54 known victims included in the 1943 Hoyanger epidemic, 19 were treated in a hospital a total of 45 months. In the words of the reporter "the Hoyanger epidemic of 1943 shows how a tuberculosis epidemic which flashes from clear skies, can shake a community" which in previous years had shown only a light morbidity. The author contrasted Aksel Taering with "Typhoid Mary" who infected with typhoid

53 persons during a period of many years. Aksel infected with tuberculosis 54 persons in a single month. Two points about this epidemic of "'Aksel the Consumptive" are worthy of emphasis. All the persons in the involved communities had been tuberculin tested and their reactions properly recorded. The population was predominately negative. Without this prior tuberculin testing and recording it would not have been possible to discover the newly infected persons. The second point that needs emphasis is that many of those infected manifested clinical tuberculosis within a short time after the infection.

Epidemic of Tuberculosis in a State School for Girls as recorded by T. V. Hyge in 1947: observation period of about three years.

In a State School for young girls about five weeks after the obligatory annual examination for tuberculosis an epidemic of tuberculosis broke out in an explosive manner becoming almost of "experimental character." Among the 368 pupils, about 12 to 18 years old, there were originally 130 tuberculin positive, 133 BCG vaccinated with positive take, 105 tuberculin negative to 1/500 mg. PPD or 100 T.U. One Calmette vaccinated girl became a converter. Of the 105 tuberculin negative pupils, 94 of whom were exposed to the infection, 70 (74.5 per cent) became converters, that is, were infected; 41 (58.6 per cent) converters showed lesions in the chest and 37 of these showed positive bacilli on gastric lavage, all of the human type; while 36 showed definite pathological x-ray film changes. In six (14.6 per cent) of these converters subsequently progressive pulmonary tuberculosis developed making employment of pneumothorax advisable. One of these patients died after pronounced generalization of disease. The tuberculous changes in connection with the primary infection were: erythema nodosum in eight cases, pleurisy three to eleven months after infection in 10, pericarditis in one and peritonitis in one. The primary infiltrations were found chiefly in the infraclavicular region and in the middle lung field appearing as a rule about three months after the infection. The instances of pulmonary tuberculosis proper, although all together 9 among 94 who had been exposed to the infection (9.6 per cent) developed in pupils 16 to 18 years of age arising from initial foci which appeared 6 to 12 months after the infection, with the exception of two in whom the primary focus seemed to have been the point of origin for the pulmonary tuberculosis. It has not been possible to establish that the primarily infected gastric lavage culture positive pupils were infective. No less than 32 tuberculin negative sibs of these latter pupils remained tuberculin negative at least for six months and then they were given BCG at their own request.

Among the 133 Calmette vaccinated pupils, 106 of whom had been exposed to the infection, two cases of pulmonary tuberculosis appeared about one year after the infection with cavity formation making employment of pneumothorax advisable, that is 1.9 per cent or two out of 106 persons. Also the Calmette vaccinated converter had pulmonary tuberculosis about one year after the infection. The infected Calmette vaccinated girl showed no primary infection.

Among the 130 initially tuberculin positive pupils, 105 of whom had been exposed to the infection, pulmonary tuberculosis developed in four, all showing positive tubercle bacilli on gastric lavage. Only two of these cases, however, could be looked upon as instances of exogenous reinfection, that is two out of 105 (1.9 per cent of the exposed). The source of infection was demonstrated to be a female teacher in whom the presence of pulmonary tuberculosis had not been realized and her active lesion was recognized on employment of tomography and gastric lavage examination.

The quarters where the infection was transmitted in this epidemic were some relatively small classrooms in the basement of the school, especially a permanently blacked-out physics room which also served as an air raid shelter and thus was lacking in ventilation as well as daylight. Under such conditions air infection with tubercle bacilli may show a surprising spreading and virulence.

Comment

Infectivity may be present in persons, who on ordinary x-ray film examination present apparently healed processes and tomography may have to be employed in order to reveal the presence of cavity. The finding of cavities must be decisive with regard to the infectivity of the patient even though gastric lavage yields but a slight positive result. This school epidemic illustrates strikingly the great risk to tuberculin negative persons. It shows plainly that the immunity acquired by an earlier spontaneous infection as well as the immunity acquired through the BCG vaccination offer a strong protection against tuberculosis. On exposure to particularly virulent infection the immunity may break down and the development of disease may result. The following summarized this epidemic.

368 School Girls 12-18 Years Old

130 originally pos. T.T.	105 originally neg. T.T.	133 pos. after BCG
4 developed TB later	70 "converters"	2 developed TB later

41 or 58.6 per cent developed TB later

Discussion

Without doubt, surgery is saving many moderately and far-advanced cases of tuberculosis but, although a small percentage of minimal cases are subject to excisional surgery in the hope of preventing later relapse, much of surgery for tuberculosis today is "salvage." As one distinguished British surgeon puts it, radical surgery for advanced tuberculosis today is "demolition squad" work. A lung is "shot to pieces" and the demolition squad steps in to tidy up and salvage life and if possible able-bodiedness. The emphasis has changed from prolonged bed rest, reversible and irreversible collapse therapy to modified rest, excisional surgery and chemotherapy. It is my earnest conviction that we should now change to routine tuberculin testing beginning at one year of age, x-ray of recent converters, close supervision of recent converters for the next three years at least, routine chemotherapy of recent converters among highly ex-

posed groups, namely, children in tuberculous families, medical students, trained nurses, hospital personnel, and finally chest x-rays not only of all hospital admissions but periodic x-rays of the chests of all persons visiting doctor's offices. Radical surgery, either collapse or excisional surgery, is life saving for many cases. The place of excisional surgery for minimal tuberculosis in this chemotherapeutic era remains to be determined. The sanatorium is and should remain an indispensable part of our plan of control of tuberculosis.

SUMMARY

The whole purpose of this summary review of some previously reported small epidemics of tuberculosis has been to emphasize the following points which I believe to be implicit in adequate control of tuberculosis. First, routine use of the tuberculin test, which reveals recent converters (ideal cases for chemotherapy) and therefore those most likely to manifest signs and symptoms of active tuberculosis within a short period of time, secondly, the indispensable value of the x-ray film to reveal lesions within the thorax undetectable by any other means; thirdly, the menace of just one unrecognized case of active pulmonary tuberculosis in a tuberculin negative community, and fourthly, the "chain reaction" nature of the spread of tuberculous infection.

RESUMEN

El propósito de esta breve exposición de algunas epidemias tuberculosas pequeñas antes relatadas, es enfatizar los puntos siguientes de importancia: Primero, hacer la investigación de rutina por la tuberculino-reacción para descubrir los casos recien virados que son los ideales para quimioterapia, y por tanto los que tengan síntomas de tuberculosis activa a breve plazo. Segundo, el uso indispensable de la película de rayos X para descubrir los casos que no se pueden encontrar de otra manera. Tercero, la amenaza que significa un caso de tuberculosis no reconocida, siendo activa, en una comunidad negativa a le tuberculina y Cuarto, la diseminación de la tuberculosis por un mecanismo de "reacción en cadena."

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Long Term Antimicrobial Therapy Without Collapse: 300 Cases of Pulmonary Tuberculosis Treated for One Year or Longer*

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Of mounting importance in recent years has been the increase of pulmonary tuberculosis among older persons, particularly white males. The advancing age of newly reported cases is recognized by many authorities as "the most significant recent trend in the epidemiology of tuberculosis."[1, 2, 3] Nearly three-fourths of all adult white male admissions to Maybury Sanatorium in 1953, for example, were over 40 years of age; over one-half were more than 50, and more than one-quarter were over 60 years of age.

The treatment of pulmonary tuberculosis in these older individuals carries with it definite clinical problems. Not the least of these is the lessened response of the older patient to antimicrobial therapy.[4] Pulmonary lesions in these individuals tend to have a more productive, fibrotic or fibrocavernous nature with less of an exudative component and, as such, respond less well to chemotherapy. Lowering of pulmonary function by the destruction of lung tissue, fibrosis and emphysema often impairs the ability of the older patient to tolerate minor or major collapse procedures or resectional surgery.[5]

As a result of these various factors, sanatorium beds are being occupied in ever-increasing number by older individuals, mostly white males, the nature and extent of whose disease places them in a definite salvage category.

Material and Methods

Between July and October, 1951, at Maybury Sanatorium, 60 of these salvage patients were placed on long-term continuous antimicrobial therapy without collapse in the hope that a certain number might be rendered noninfectious and that at least a few might be prepared for discharge from the sanatorium. For the most part they were white males over 40 years of age with far advanced, bilateral, fibrocavernous disease of long standing: patients with poor prognosis who had failed to respond to the then accepted standards of therapy. With persistence in this practice a total of 137 salvage patients now have received continuous antimicrobial therapy for one year or longer without collapse.

Similarly treated since 1951 are 163 with less advanced, less fibrotic, less destructive disease of shorter duration, our so-called nonsalvage or regular type of admission. This is the group in which drug therapy, with or without surgery, was expected to be definitive.

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The rather interesting comparison in the response of these two groups to long-term antimicrobial therapy without collapse forms the subject matter of this paper.

All of the 300 patients here reported received continuous antimicrobial therapy for 12 months or longer with no collapse procedures or surgical intervention. Those who were discharged or surgically treated before the completion of the full year of antimicrobial therapy are not included in this study.

No attempt is made to assess the relative efficacy of the various antimicrobial regimens employed. The early patients in both groups were treated with streptomycin, one gram two or three times weekly, and para-aminosalicylic acid (PAS) 12 grams daily. As isoniazid became available, this agent was added to the treatment regimen in many instances (in doses of from three to five miligrams per kilogram of body weight). Later, some patients received isoniazid and PAS initially. In a few cases, streptomycin and isoniazid were used as the initial treatment regimen. Therapy in all instances, however, was combined and continuous.

Composition of Study Groups

There were sharp differences in the composition of the salvage and nonsalvage groups.

The salvage group was composed largely of white males (76.6 per cent) while the nonsalvage group represented a more typical cross section of the general adult sanatorium population as regards color and sex (Table I).

TABLE I—COLOR AND SEX

	MALE				FEMALE					
	White		Non-White		White		Non-White		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Salvage	105	76.6	12	8.8	12	8.8	8	5.8	137	100
Nonsalvage	87	53.4	28	17.2	26	15.9	22	13.5	163	100

Nearly three-fourths of the salvage patients were over 40, nearly half of them over 50 years of age (Table II). The nonsalvage patients, however, were distributed almost equally between those over and those under 40 years, and only one-third were over 50 years of age.

TABLE II—AGE

	30 years		31-40 years		41-50 years		51-60 years		60 years		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Salvage	13	9.5	23	16.8	34	24.8	36	26.3	31	22.6	137	100
Nonsalvage	44	27.0	29	17.8	30	18.4	33	20.2	27	15.9	163	100

The salvage patients had much more advanced disease. Almost 90 per cent were classified as far advanced, 10 per cent were moderately advanced, and there was no minimal case (Table III). Only 53 per cent of the nonsalvage patients had far advanced tuberculosis, 40 per cent were

moderately advanced, and 7 per cent were classified as having minimal disease. Over 27 per cent of the nonsalvage patients had unilateral involvement, as against only 2 per cent of the salvage group.

TABLE III—CLASSIFICATION OF DISEASE

	MINIMAL		MOD. ADVANCED				FAR ADVANCED					
			Unilateral		Bilateral		Unilateral		Bilateral		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Salvage	0	0	2	1.5	12	8.8	1	0.7	122	89.1	137	100
Nonsalvage	12	7.4	19	11.6	46	28.2	14	8.6	72	44.2	163	100

Also, the duration of disease before treatment was longer among the salvage patients (Table IV). Nearly 87 per cent had had their disease for one year or longer, as compared with only 45 per cent among the nonsalvage patients. More than one-fourth of the latter group had developed tuberculosis less than six months prior to treatment; in the salvage group only 4 per cent had disease of this short duration.

TABLE IV—DURATION OF TUBERCULOSIS

	6 mos.		6-12 mos.		1-2 years		2-5 years		5 years		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Salvage	5	3.6	13	9.5	30	21.9	41	29.9	48	35.1	137	100
Nonsalvage	42	25.7	48	29.4	34	20.9	31	19.1	8	4.9	163	100

The salvage group had much more destructive disease (Table V). Over 63 per cent had cavities totaling 4 cm. or more in diameter, as compared with only 27 per cent in the opposite group. Almost 14 per cent of the salvage patients had total cavitation greater than 10 cm. at the start of treatment; there was no patient with such extensive cavitation in the nonsalvage group.

TABLE V—CAVITATION

	NO CAVITATION		CAVITATION							
			Total Cavit.		Under 4 cm.		4-10 cm.		Over 10 cm.	
	No.	%	No.	%	No.	%	No.	%	No.	%
Salvage	20	14.6	117	85.4	30	21.9	68	49.6	19	13.9
Nonsalvage	33	20.2	130	79.8	86	52.8	44	27.0	0	0

Ninety per cent of the salvage patients were positive for tubercle bacilli on direct examination of the sputum, an additional 4 per cent by culture (Table VI). In contrast, 70 per cent of the nonsalvage group were positive on direct examination, and an additional 13 per cent on culture.

TABLE VI—SPUTUM

	NEGATIVE		POSITIVE					
			Total Positive		Direct Exam.		Culture Only	
	No.	%	No.	%	No.	%	No.	%
Salvage	9	6.5	128	93.5	123	89.8	5	3.7
Nonsalvage	28	17.2	135	82.8	115	70.1	20	12.7

Almost 47 per cent of the salvage patients had had prior collapse therapy, antimicrobial therapy or both (Table VII). Only 11 per cent of the nonsalvage group had had previous treatment.

TABLE VII—PRIOR TREATMENT

	NO PRIOR TREATMENT		PRIOR TREATMENT							
			Total Prior Rx		Collapse		Anti-Microbials		Both	
	No.	%	No.	%	No.	%	No.	%	No.	%
Salvage	73	53.3	64	46.7	17	12.4	13	9.5	34	24.8
Nonsalvage	145	89.0	18	11.0	6	3.7	4	2.4	8	4.9

Summarizing, it may be said that the salvage patients (as compared with the nonsalvage) were older individuals, mostly white males, with more advanced, more destructive disease of longer duration, nearly half of whom had failed to respond satisfactorily to previous treatment with collapse or drugs or both.

Results of Therapy

As of December 15, 1953, the results of long-term continuous antimicrobial therapy in these two groups were analyzed as regards x-ray film changes, cavity closure, sputum conversion, and present status. In each group at that date, the longest period of observation in the sanatorium under continuous drug therapy was 30 months. The average duration of treatment among the salvage patients was 20.5 months; in the nonsalvage group 16.6 months.

At observation periods of three, six, nine and 12 months all of the 137 salvage and 163 nonsalvage patients were in the sanatorium receiving antimicrobial therapy. Still in the sanatorium under continuous therapy and observation at 15 months were 122 salvage patients and 131 nonsalvage; at 18 months 94 and 70 respectively, at 24 months 65 and 29. Too few patients(16) were observed for longer than 24 months to make the data significant. Results of therapy at the stated observation periods are based on the above numbers of patients.

X-Ray Changes

Comparing serial progress films with the initial film at the start of treatment, evaluation was made of the percentage change in the extent and density of infiltrations. As far as possible changes due to variation in cavitation were discounted. Changes in infiltration were tabulated under four headings: worse, zero to 30 per cent improvement, 31-60 per cent improvement, and greater than 60 per cent improvement. As shown in Figure 1, infiltrations in the nonsalvage group cleared much more rapidly and completely. At 12 months, nearly 70 per cent of the nonsalvage cases had shown significant (i.e., more than 30 per cent) clearing of infiltrations, as contrasted with only 24 per cent of the salvage cases. At 24 months, infiltrations had cleared significantly in nearly 86 per cent of the nonsalvage group but in only 32 per cent of the salvage. The difference in the proportion who showed marked (i.e., greater than 60 per cent)

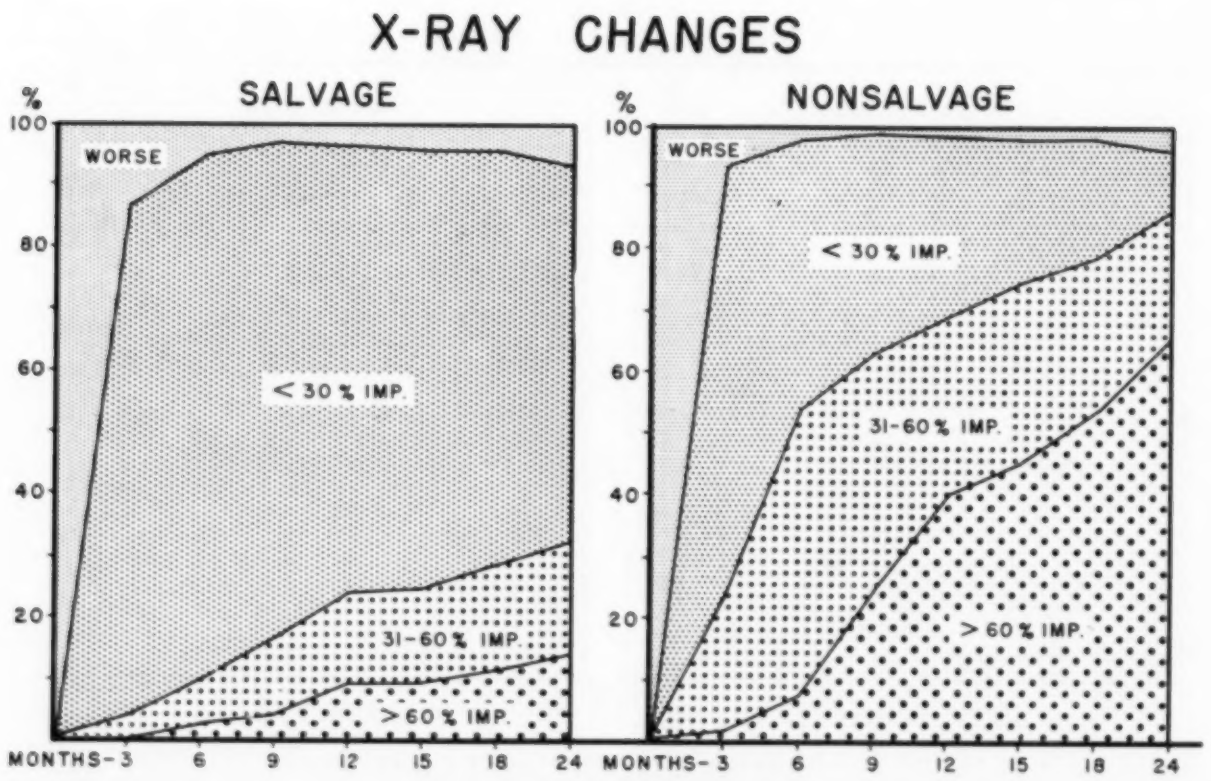
X-RAY CHANGES
SALVAGE
NONSALVAGE
%
100
80
60
40
20
WORSE
< 30 % IMP.
31-60 % IMP.
> 60 % IMP.
MONTHS-3
6
9
12
15
18
24

FIGURE 1

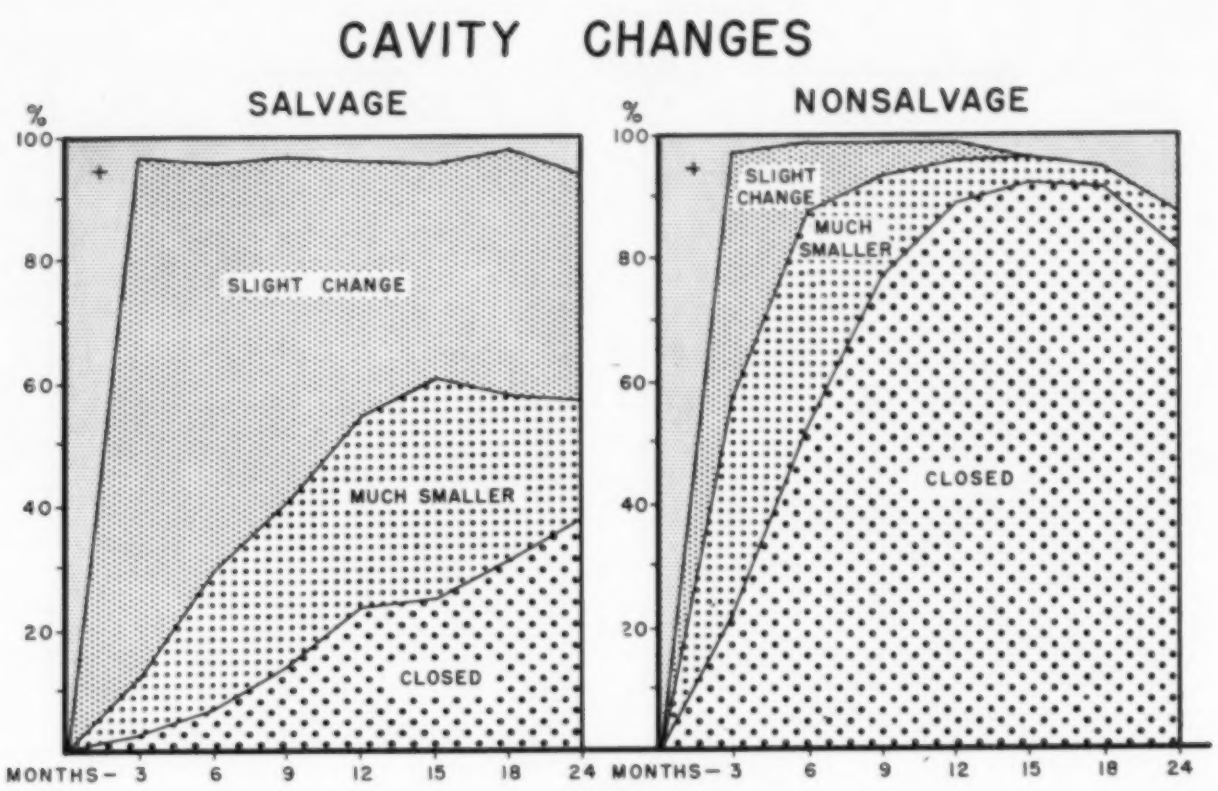
CAVITY CHANGES
SALVAGE
NONSALVAGE
%
100
80
60
40
20
SLIGHT CHANGE
MUCH SMALLER
CLOSED
MONTHS— 3 6 9 12 15 18 24

FIGURE 2

improvement was even more striking. At 24 months for example, 66 per cent of the nonsalvage and only 14 per cent of the salvage cases had shown marked resolution of infiltrations. The number which worsened during therapy was somewhat, but not strikingly, higher in the salvage group; in the six to 18 months' period, the number varied between 3 and 5 per cent in the salvage and between 0.6 and 2 per cent in the nonsalvage cases.

Cavity Closure

The difference in cavity closure in the two groups was equally marked. At the beginning of treatment 117 of the 137 salvage cases (roughly 85 per cent) had cavitation (Table V) as compared with 130 of the 163 nonsalvage cases (80 per cent). In serial progress films, evaluation of cavity size was made under these headings: larger, no change or slightly smaller, much smaller, and closed. Figure 2 shows the striking difference in the response of the two groups as regards cavity closure. In the nonsalvage group at six, 12 and 18 months respectively, cavities were read as closed in 41, 79, and 93 per cent. Among the salvage cases at the same intervals, however, only seven, 23, and 31 per cent had closed cavities. A sizable additional number of the salvage group were read as having cavities much smaller at the above intervals of time but nearly 40 per cent of the salvage cases had little or no change in cavity size throughout the course of treatment. Cavities were read as larger in approximately the same proportion of cases in each group (between 2 and 5 per cent) during the first 18 months of therapy.

Sputum Conversion

Despite the marked contrasts as regards x-ray change and cavity closure, the difference in sputum conversion between the two groups was surprisingly slight (Figure 3). At the start of therapy, 83 per cent of the nonsalvage and 94 per cent of the salvage patients were positive on culture. The nonsalvage patients converted considerably more rapidly so that by the ninth month 88 per cent of them and 71 per cent of the salvage patients were negative by culture. With further chemotherapy few additional nonsalvage patients converted their sputum, but the conversion rate among the salvage patients continued to climb. By the 18th month, 80 per cent of the salvage and 92 per cent of the nonsalvage patients were negative by culture, a striking tribute to the effectiveness of chemotherapy in converting sputum even in the face of such massive disease as is represented by the salvage group. Moreover there were surprisingly few bacteriologic relapses. A total of 232 patients in the two groups achieved consistently negative cultures by the 12th month. Of the 201 in this category who continued in the sanatorium under further chemotherapy and observation, only 10 (5 per cent) suffered bacteriologic relapses as evidenced by positive culture or smear in a subsequent observation period.

Status of Patients

As might be expected there are sharp differences in the present status of the two groups (Table VIII). As of December 15, 1953, 32 per cent

TABLE VIII—STATUS DECEMBER 15, 1953

	DISCH.		ABSC.		TRANSF.				DIED				IN SANATORIUM		TOTAL	
					Surgery		Other		Tbc.		Other					
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Salvage	8	5.8	11	8.0	2	1.4	7	5.1	2	1.4	5	3.6	102	74.4	137	100
Nonsalvage	52	31.9	22	13.5	31	19.0	7	4.3	1	0.6	0	0.0	50	30.7	163	100

of the nonsalvage patients had been discharged as arrested, as against only 6 per cent of the salvage group. Nineteen per cent of the nonsalvage and only one and a half per cent of the salvage patients had been transferred for surgery (resection and thoracoplasty). There was one death in the nonsalvage group, 24 hours following resectional surgery. There were only two deaths from tuberculosis among the salvage patients, the first with overwhelming terminal disease at the 14th month of observation, two months after refusal of further therapy; and the other largely a circulatory death secondary to long-standing pulmonary fibrosis and emphysema at the 19th month of treatment. Five salvage patients died from nontuberculous causes: two with coronary thrombosis; one, acute

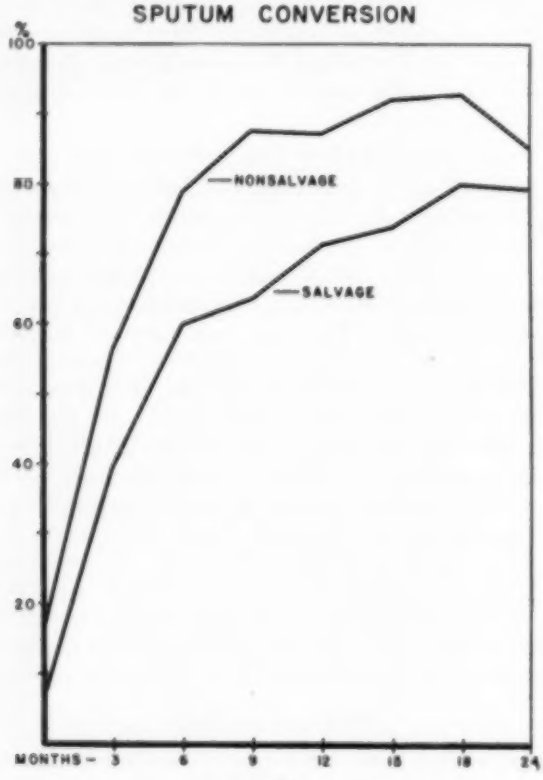

FIGURE 3

glomerular nephritis; one, subleukemic leukemia; and one by suicide. The paucity of tuberculous deaths among the salvage group illustrates the fact that if patients do not die with overwhelming tuberculosis within the first three months of treatment, they are likely to die from causes other than tuberculosis. Nearly three-fourths of the salvage and less than one-third of the nonsalvage patients were still in the sanatorium as of December 15, 1953. Interestingly, the salvage patients appeared to accept sanatorium treatment better than did their counterparts as evidenced by the fact that the proportion of irregular discharges among the salvage patients was nearly 50 per cent lower than among the nonsalvage group.

Discussion

Long-term antimicrobial therapy was applied to two classes of patients in this study. In the nonsalvage group with less destructive disease, the objectives of therapy were the usual ones: cavity closure, sputum conversion and preparation for discharge or definitive surgery. In the majority here reviewed these objectives were reached fairly rapidly and completely.

Among the salvage patients, however, the aims of treatment were quite different. The advanced, bilateral, destructive nature of their disease precluded hope of early discharge or surgical attack. In many instances, destruction of lung tissue was so great that it would have been genuinely unrealistic to aim for complete restoration of health. Rather, we set up for these patients a modified objective: the establishment and maintenance of a state of noninfectiousness which not only would protect the sanatorium personnel but which, in certain instances at least, would allow the patients' return to more or less normal living conditions at home without hazard to others. As was expected, radiographic response in these salvage patients has not been great. Spreads and x-ray deterioration, however, have been marked by their relative absence; clinical and symptomatic improvement has been gratifying and deaths from tuberculosis have been astonishingly few. Under prolonged therapy, moreover, sputum conversion by culture has been achieved in over three-fourths of these individuals and there have been surprisingly few bacteriologic relapses. Actually, for these poor prognosis patients, the achievement of stable roentgenograms, negative sputum cultures and acceptable clinical status represents a goal which in the pre-chemotherapeutic era was considered highly satisfactory for *all* patients and should constitute today a primary objective in treating this growing class of sanatorium patients.

A sizable number of these salvage patients are now at the point where discharge to the outpatient department for further chemotherapy seems feasible. A large proportion of the salvage group, however, are homeless, indigent, elderly men with massive residual disease. For many of them, continued institutional care is obligatory. At Maybury Sanatorium, we are now redesigning a building—The Club, as we term it—where under medical supervision these patients may enjoy the privileges of recreational facilities, occupational therapy, rehabilitation and outdoor exercise, with antimicrobial therapy maintained.

For the patient whose disease has stabilized but still is of such proportion that therapy must be extended indefinitely, we have developed the concept of a maintenance dose: the lowest dose of antimicrobials which will preserve the therapeutic effects already obtained. Roughly the use of a maintenance dose of antimicrobials in tuberculosis is analogous to that of insulin in diabetes and digitalis in cardiac decompensation. In both of these latter disorders, once the acute symptoms have been controlled and the disease process has been stabilized, the therapeutic agents are used for maintenance purposes in doses which at the start would have been subtherapeutic. Presently at Maybury Sanatorium, 26 salvage patients are receiving maintenance therapy. In 24 this consists of one gram of streptomycin weekly with 200 to 300 mgm. of isoniazid daily; one receives 1 gram of streptomycin weekly with 6 grams of PAS daily; and the other receives 6 grams of PAS with 200 mgm. of isoniazid daily. All had major residual disease when maintenance therapy was started. Roentgenographically, all lesions had been stabilized from six to 30 months, an average of 13.0 months. Cultures had been negative from three to 26 months, an average of 15.4 months. During an observation period of three to 12 months on maintenance therapy, only one worsened roentgenographically, a silicotic who opened a filled cavity but still remained negative repeatedly on culture. One of the 26 became positive on culture (one month after maintenance therapy was started) but serial roentgenograms have shown no deterioration. In the other 24 the original radiologic and bacteriologic gains were preserved under maintenance therapy. A more detailed study will be reported later. At this time, however, we feel that maintenance therapy in selected cases is a promising means of preserving therapeutic gains in patients with massive residual disease.

SUMMARY

The advancing age of sanatorium populations carries with it definite clinical problems. Since 1951 at Maybury Sanatorium, 137 poor prognosis, salvage patients have been treated with long-term antimicrobials. They were older white males, for the most part, with far advanced fibrocavernous disease of long standing. Results are compared with 163 similarly treated patients with less destructive disease of shorter duration. As regards cavity closure, x-ray improvement and time of discharge, the salvage group lagged far behind the nonsalvage. But in sputum conversion, the salvage group was only slightly less impressive. The achievement of stable roentgenograms, negative sputum cultures and acceptable clinical status in over three-fourths of their number justifies the prolonged use of antimicrobials in individuals with apparently poor prognosis. For the patient whose disease has stabilized but still is of such major proportion that therapy must be extended indefinitely, the concept of a maintenance dose is introduced. Such therapy in selected cases is a promising means of preserving therapeutic gains.

SUMARIO

El aumento en la edad de la población sanatorial se acompaña de problemas clínicos definidos. Desde 1951 en el Maybury Sanatorium, han sido

tratados por largo tiempo con antimicrobianos 137 pacientes de rescate con pronóstico muy serio. En su mayoría eran hombres blancos viejos, con enfermedad muy avanzada de tipo fibrocavernoso delarga duración. Se comparan los resultados con 163 pacientes con padeciemiento menos destructivo y de más corta duración que fueron tratados de igual manera. Los pacientes del primer grupo sobrepasaron-con mucho en tiempo a los pacientes del segundo para cerrar sus cavernas, obtener emjoría radiológica y ser dados de alta. Pero con respecto a la conversión del esputo, sólo hubo ligeras diferencias. La obtención de radiografias estables, cultivos de esputo negativos y un estado clínico aceptable, en más de las ¾ partes del grupo—justifica el uso prolongado de antimicrobianos en individuos que aparentemente tienen pronóstico pobre. Se introduce el concepto de dosis de mantenimiento para aquellos pacientes en quienes se ha estabilizado su enfermedad pero aún reviste grandes proporciones, lo cual obliga a continuar el tratamiento indefinidamente. Tal conducta encasos seleccionados permite conservar la mejoría terapéutica obtenida con anterioridad.

RESUME

L'augmentation de l'âge moyen des malades hospitalisés en sanatorium entraine des problèmes cliniques prècis. Depuis 1951 au Sanatorium de Maybury, 137 malades de pronostic réservé, ont été traités par les médications antimicrobiennes, longtemps prolongées. Pour la plupart, ils'agissait de malades assez âgés, de race blanche de sexe masculin, porteurs de lésions fibro-excavées avancées, et très anciennes. On a comparé les résultats à ceux obtenus chez 163 malades traités de la même façon, mais qui étaient atteints de lésions moins destructrices et beaucoup plus récentes. En ce qui concerne la fermeture des cavités, l'amélioration radiologique et le temps d'hospitalisation, le "groupe de dépannage" était très en retard par rapport à l'autre. Mais en ce qui concerne la négativation des expectorations, le "groupe de dépannage" ne fut guère moins impressionnant. La tendance à la stabilité radiologique, la négativation des cultures, et le bon état général des malades pour à peu près les trois-quarts d'entre eux, justifient l'utilisation prolongée des médications antimicrobiennes chez des individus dont le pronostic était apparemment très sérieux. Pour le malade dont l'affection a été stabilisée mais que néanmoins nécessite encore la continuation indéfinie de la thérapeutique, les auteurs introduisent la notion d'une dose d'entretien. Dans des cas choisis, une telle thérapeutique est un procédé remarquable pour éviter la saturation thérapeutique.

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The Role of Bronchoscopy in Tuberculosis of Infancy and Childhood*

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Although the use of the bronchoscope in tuberculosis among children has been the subject of a number of communications in recent years, the exact role of this procedure has not been defined. Especially is this true since the advent of antibiotics and chemotherapeutic agents. The present report is offered not as a reduplication of work which has gone before but to emphasize the value of continued exploration and a new approach to a situation which already has received attention.

Infants and children in this series were selected at random with the sole pre-requisite that they have active tuberculosis, diagnosed on a strongly presumptive or bacteriologically proved clinical status. The employment of bronchoscopy beyond this consideration was essentially at random and without regard for the usual criteria of endobronchial disease such as atelectasis, lobar or segmental distribution, wheeze, cough, or bacteriologic findings.

The series consisted of 37 children on whom 79 bronchoscopies were performed by one of us (HJR). These patients were chosen as indicated from a total group of approximately 80 children seen with tuberculous endothoracic disease at the Los Angeles County General Hospital from September, 1951, to December, 1953.

Technique

After a few initial frustrating bronchoscopies with no anesthesia, all children subsequently were examined under general anesthesia. We are in strong agreement with others[1, 2] that there is no substitute for complete relaxation in these children, and this is assured by general anesthesia. Without such relaxation it is impossible to inspect each segmental orifice in a child because of violent expulsive efforts associated with struggling and coughing. The bronchus collapses over the mouth of the tube, and not more than a hasty unsatisfactory glimpse on inspiration is possible. Without anesthesia there is the additional hazard of traumatizing mucus

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membrane, thereby favoring the initiation or extension of endobronchial disease.

Rectal barbiturates[2, 3] are reported to be excellent, but in our hands open drop ether has proved equally satisfactory. Return of consciousness is rapid and the period of immediate postoperative observation by trained personnel shorter. Vinethene induction is followed by ether, and anesthesia is carried down to the second plane of the third stage. The anesthetist steps aside and the bronchoscope is introduced. It is unnecessary to insufflate ether through the bronchoscope because children remain without a significant cough reflex sufficiently long to permit unhurried examination and the taking of specimens. Upon withdrawal of the bronchoscope there is no laryngospasm. A mouth airway is inserted, the child is turned prone, and general management is the same as that following anesthesia for adenotonsillectomy. Recovery is rapid. This form of anesthesia is well tolerated, and there has been no evidence of aggravation of the pulmonary disease.

Postbronchoscopic subglottic edema has not been encountered because instrumentation is gentle and the bronchoscopes of proper size. Selection of the correct bronchoscope is most important. Generally speaking it is better in this type of examination to use a bronchoscope slightly smaller than that recommended for a given age. For example, a foreign body in a main stem bronchus of a 20-month-old infant can best be visualized and grasped through a 4-mm. bronchoscope. However, a 3½-mm. bronchoscope would be more suitable for examination of a tuberculous child because it better exposes the orifices of the segmental divisions of the lower lobes. The smaller bronchoscope can be insinuated farther and hence more can be seen. Particularly in the presence of any narrowing of the lumen of a main stem bronchus by disease is the smaller bronchoscope superior. It is not sufficient to inspect only the trachea and main bronchi. All orifices, including the primary segmental ones, can and should be inspected individually.

Results

As indicated, the patients were selected essentially at random and were subsequently classified as bronchoscopically positive or bronchoscopically negative. Positive findings were limited to the presence of visible granulations, marked compression by external pressure, and severe orificial inflammatory stenosis. Redness of the mucosa and/or presence of purulent secretions were not considered evidence of specific disease and, although undoubtedly related to the underlying tuberculosis, were classified as not showing specific pathology.

The positive group consisted of 12 patients; seven of these had endobronchial granulomas, four had marked stenosis from external pressure, and one had severe inflammatory stenosis of the right middle lobe orifice. Of these 12 the average age was 33 months; six were 12 months or younger; the oldest was 48 months. Six were Negroes, three Latin Americans, two Caucasians, and one Oriental. Six (50 per cent) had positive identified con-

tact history with open tuberculosis, usually in the immediate family. Six (50 per cent) had positive gastric cultures. Only 25 per cent of the known contact cases proved to be bacteriologically positive. In addition to the six who were positive by gastric culture, two yielded positive cultures on bronchoscopic aspiration. Four (33 per cent) had persistent cough to suggest endobronchial disease. No frank sign of endobronchial disease was recorded in the ward officer's examination.

On x-ray film inspection, four had atelectasis of all or part of the right lower or middle lobe to suggest the presence of endobronchial disease. On the other hand, eight had merely confluent infiltrations or mass-like lesions which could not satisfy the criteria of atelectatic processes. Three of these were in the left upper, three in the right middle, one in the right upper, and one in the right lower lobes.

Comparing this positive group with the bronchoscopically negative there is little significant difference. The average age was 29 months and eight (34 per cent) 12 months or younger. Eleven were Negroes, seven Latin Americans, and seven Caucasians. Twelve (48 per cent) had positive history of contact, usually in the immediate family and these made up 66 per cent of the 12 who were bacteriologically positive on gastric culture. Cough of important severity or persistence was present in 25 per cent. No marked physical finding was recorded. X-ray studies disclosed shadows that satisfied criteria for atelectasis of a lobe or segment in eight patients. Six of these were in the upper lobes. Confluent infiltrative or mass-like shadows were seen in 13, calcifying hilar nodes in one, and unilateral emphysema and pleural effusion in one each.

In general, neither the historical, racial, nor bacteriologic findings seemed to distinguish the bronchoscopically positive and negative groups. Likewise the physical findings, symptoms, and x-ray shadows while generally recommended as a basis for distinction, did not seem to offer a means of differentiating between the two groups.

The bronchoscopic findings in the 12 bronchoscopically positive cases are summarized as follows:

Case 1: Age two years. The carina was greatly broadened, reducing the origins of both main stem bronchi to slits. As the bronchoscope was advanced, the medial walls of both main bronchi yielded easily to pressure. All of the usual orifices were identified and were clear. As the bronchoscope was withdrawn, the origins of the main bronchi again assumed their slit-like appearance. There was no endobronchial disease, the deformity being due to soft, enlarged mediastinal lymph nodes. (This child had a severe wheeze and stertorous respirations that could be heard down the hall.) Five weeks later all evidence of disease had cleared, and the carina had resumed its normal appearance.

Case 2: Age six months. The carina was broad. The bronchoscope was advanced on the right and no abnormalities noted. On the left the main stem bronchus was narrowed, and about ½ cm. below the carina a large amount of pus suddenly welled up and obscured vision. Repeated aspiration was followed by reappearance of pus until finally visibility was restored. The main stem bronchus was now much more patent, and pus was seen to be escaping in a constant trickle from a pin-point opening on the medial wall of the bronchus 1 cm. below the carina. The remainder of the bronchus and its orifices were clear. This of course represented a suppurating mediastinal lymph node which was pointing, and pressure of the bronchoscope caused rupture into the main bronchus.

On re-examination three weeks later the left main stem bronchus was of normal patency. At the site of perforation a small nubbin of pale inactive looking granulation

tissue was present which was not disturbed. There was no pus. On final examination seven weeks after the initial one the tracheobronchial tree appeared normal.

Case 3: Age six months. The carina was broadened, the fullness extending down the right main stem. At the level of the middle lobe orifice the main bronchus was reduced to a slit, the medial wall almost contacting the lateral. At this point the mucous membrane was granular, bled easily, and was studded with flecks of exudate which could not be detached with suction. Bronchoscopy two months later showed no change. Final examination seven months after the first showed complete resolution of disease. The stenosis here was principally the result of deformity by extrinsic pressure rather than by endobronchitis.

Case 4: Age eight years. Just below the level of the right upper lobe orifice the main stem bronchus was occluded by a soft, easily bleeding granuloma. A suction tip was forced past it and at once aspirated in a steady stream over a half ounce of heavy green pus which had been trapped behind the granuloma. This was partially removed with forceps, bleeding obscuring the field. Two weeks later the granuloma previously noted was seen to arise from the medial wall of the main stem bronchus. It was forced aside, and the bronchoscope advanced to the base. A large amount of pus was again aspirated. The lower segmental orifices were identified and free of disease. The surface of the granuloma was rubbery and could not be grasped so that only a small piece could be removed.

One month after the initial bronchoscopy there was complete resolution of active disease, and the nature of the previous observations became clear. From just below the middle lobe orifice to the base the main stem was severely distorted by fullness of the medial wall due to extrinsic pressure. What previously appeared to be entirely granuloma was only partially so, much of it representing underlying bronchial wall which had been pushed medially by diseased mediastinal lymph nodes. The mucous membrane had completely healed, but the bronchus was narrowed. The child was discharged home and not bronchoscoped again as permission was refused. Judging from observations on other children, the bronchus may be expected to regain its normal caliber.

Case 5: Age four years. The mucus membrane of the right main stem bronchus was injected as compared with the left, and pus escaped from the upper lobe. Granulation tissue, which bled on touch, covered the spur of the right upper lobe bronchus. The orifice itself did not appear to be obstructed by disease. Examination three months later revealed no evidence of disease.

Case 6: Age four years. Just below the right upper lobe orifice the main bronchus was filled by a large, soft, easily bleeding granuloma. This was grasped with fenestrated mosquito forceps and removed piece meal. The middle lobe orifice was then visualized and seen to be patent. The granuloma arose from the most medial portion of the middle lobe bronchus and the adjacent main bronchial wall. Two weeks later the granuloma was smaller, paler, and flapped back and forth on respiration. It was again removed. On final examination six weeks after the first, all evidence of endobronchial disease had disappeared.

Case 7: Age 18 months. The middle lobe orifice was inflamed and so edematous that its lumen was reduced at least 50 per cent. Pus escaped on cough. 8½ weeks later all edema had subsided and the orifice was widely patent.

Case 8: Age two years. The right middle lobe orifice was thickened by infiltrative changes and acutely inflamed. On tilting the bronchoscope to afford better exposure a large plug of heavy inspissated solid debris popped out and was removed. This had completely obstructed the bronchus. A thin mucopurulent secretion then escaped. The lower lobe spurs were thickened and glossy but not specifically diseased. On repeated bronchoscopies the inflammatory changes involving the middle lobe orifice subsided, but it was completely filled by a granuloma which could not be removed and around which thin pus escaped. On final examination five and one half months later the granuloma still filled the lumen.

Case 9: Age two years. The right main bronchus was acutely inflamed and filled with thick green exudate so adherent and tenacious as to suggest a membrane. The bronchus was cleared with suction, and pus was seen to be escaping on cough from the middle lobe orifice. The orifice itself was inflamed and edematous almost to the point of occlusion. On aspiration two weeks later there was no significant change, but on subsequent bronchoscopies there was gradual improvement. For months the main stem was thickened, granular, bled easily, and nubbins of granulation tissue were scalped off. On final examination seven months after the initial bronchoscopy there was no evidence of disease, and the middle lobe orifice was widely patent. (Rapid improvement followed the administration of rimifon.)

Case 10: Age two and one half years. Just below the right upper lobe orifice the main stem bronchus was occluded by caseous exudate and granular thickening. The

bronchoscope was forcibly advanced and this inspissated debris aspirated. Immediately a large quantity of fluid pus escaped from below. No individual landmarks could be recognized at this time. Two weeks later there was marked improvement, exudate no longer obstructing the bronchus and a suction tip aspirating no pus. The entire mucosal surface was granular, and the lumen much narrowed. Four months later all evidence of active endobronchitis had subsided, but the right main stem from just below the upper lobe orifice was narrowed about 50 per cent as compared with the left. The child was discharged clinically free of active disease but with an apparent residual bronchial stenosis.

He was again bronchoscoped 16 months after discharge from the hospital, and both main stem bronchi were of the same caliber throughout their entire lengths. The middle lobe orifice, which had never been previously visualized, was easily identified and appeared normal, as did the basal segmental orifices. That portion of the tracheobronchial tree capable of being inspected through a bronchoscope had returned to normal.

Case 11: Age three and one half years. The orifice of the left upper lobe was acutely inflamed, edematous, and bled on touch. A small granuloma partially filled the lumen. This was removed with forceps. Three weeks later all evidence of acute inflammation had subsided. A small granuloma was again present in the orifice and was removed. On final examination five months after the first one there was complete resolution of all disease, and the left upper lobe orifice was widely patent.

Case 12: Age two years. The left upper lobe orifice was inflamed and granular practically to the point of occlusion. Membranous exudate was so thick that it blocked the suction tip and had to be picked off its end. The inspissated secretion was acting as a foreign body. One month later all inflammation and exudate about the orifice had cleared, but the lumen was completely occluded by a soft granuloma which protruded slightly into the main stem lumen. Bronchoscopy was repeated on several occasions and that portion of the granuloma extending into the main stem scalped off. All active inflammation had subsided, but the lumen was completely filled by granuloma. (On x-ray film inspection the entire left upper lobe showed gradually increasing contractive changes; the child recovered clinically.)

Discussion

Consideration of the problem in the light of these findings and those who have reported before us poses two questions. Does bronchoscopy provide information that cannot be obtained otherwise, and is the information so obtained of essential importance to prognosis and therapy? The answer to both questions seems to be in the affirmative.

From our experience the existence of an atelectatic shadow will probably lead to the discovery of endobronchial disease provided the orifices to that segment or segments are accessible to the bronchoscope. Where such accessibility is not easy, as in the upper lobes and to a lesser extent in the middle lobe, it is likely that endobronchial granulations often exist beyond the scope of vision. It is therefore possible that the eight patients with atelectatic shadows in our bronchoscopically negative group simply had such lesions which could not be seen. But what is of greater significance is that eight cases showed bronchoscopic evidence of disease which could not have been predicted on the basis of clinical or x-ray data.

The frequent sequel of bronchiectatic disease as an aftermath of tuberculosis emphasizes the importance of securing early and lasting relief from such lesions. Not only do the granulations represent excrescences on the bronchial sometimes harboring tuberculous organisms, but they replace normal mucous membrane and act as nonspecific foreign bodies. Secretions distal to them cannot drain, thus setting in motion the train of events leading to atelectasis and ultimate bronchiectasis. The importance of removing them and aspirating inspissated secretion and trapped

pus cannot be overemphasized. If the mucosa is merely inflamed and granular, it will return to normal as the underlying pulmonary disease is brought under control, but formed granulomata require a more definitive approach.

The fate of this insidious endobronchial disease cannot be tied to the fate of the underlying tuberculosis and left to the beneficial effects of the antibiotics and chemotherapeutic agents. Our experience, and that of others, points to the necessity of a two-fold attack: antibiotics and chemotherapeutic agents for the underlying disease, and the endoscopic removal, as often as they recur, of endobronchial granulations.

An unsolved problem lies in the management of those granulomata beyond the reach of forceps. In several children the adjacent main stem bronchus was free of disease but obstructing granulations remained tantalizingly out of reach in the left upper or right middle lobe orifices. Herein lies the outstanding shortcoming of bronchoscopy. The segmental orifices cannot be reached and granulations at these levels cannot be removed. This may explain those instances in which the main bronchi are restored to gross normalcy, but the x-ray picture shows little or no change.

The basis of these granulations is not completely apparent. Gorgenyi[4] believes they form at or adjacent to the site of rupture of caseous mediastinal or peri-bronchial nodes and extend along the bronchial wall. The fact that they are most commonly seen on the mesial wall of the main bronchus or the mesial lips of the secondary orifices may lend some weight to this concept. Hardy[5] et al. described one patient where granulations developed at the point of rupture, and we have witnessed the development of one such granulation after observing initially the appearance of only a pin-point rupture into the left main bronchus (Case 2).

General Course of the Disease

All the patients in the negative and positive groups were on a course of antibiotic therapy during the period of observation. As a general rule the children under four received ¼ gram of streptomycin intramuscularly twice weekly, supplemented by 4 grams of PAS daily in a flavored freshly prepared oral solution. The older or larger children received .35 to .5 grams of streptomycin and 6 grams of PAS. In the event of continued fever or evidence of dissemination of the streptomycin dosage was increased temporarily to daily frequency, but rarely was the dose made larger. Children on this drug regimen with obstructive endobronchial granulomata did not show satisfactory clinical improvement until the granulations were removed and retained pus aspirated. In a few instances INH was added when progress was not as anticipated. Under this combined regimen the progress of all children observed was satisfactory and to date no disseminations in the form of miliary or metastatic disease to the meninges or other extra-pulmonary sites has occurred.

Since the fate of stenosis by pressure and inflammatory orificial stenosis is dependent on the outcome of the underlying disease, it would appear

that the continued use of these antituberculosis agents is indicated where such endobronchial evidence of disease is demonstrated.

Since this report was prepared, INH has been included in all chemotherapy.

We gratefully acknowledge the cooperation of the Department of Anesthesia.

CONCLUSIONS

1. A series of 79 bronchoscopies on 37 children with pulmonary tuberculosis is reported.

2. The children were selected at random, without particular regard for the usual criteria for bronchoscopy.

3. Twelve (32.4 per cent) had visible endobronchial disease. In seven this was manifested by granulomata, in four by deformities resulting from the pressure of enlarged mediastinal lymph nodes, and in one by inflammatory orificial stenosis.

4. Drugs alone brought about resolution of enlarged nodes and granular mucous membrane but not of formed granulomata.

5. Bronchoscopic removal of granulomata and aspiration of exudate was effective in restoring to normal appearance those bronchi visibly involved by granulomatous disease.

6. Both the x-ray and clinical signs are unreliable in determining prior to bronchoscopy which child will have visible endobronchial disease.

7. Bronchoscopy is an important adjunct in the diagnoses and treatment of children with pulmonary tuberculosis and should be performed on those in whom the total picture indicates the necessity of more than merely casual observation.

CONCLUSIONES

1. Se reporta una serie de 79 broncoscopías en 37 niños con tuberculosis pulmonar.

2. Los pacientes fueron seleccionados al azar sin atender particularmente al criterio usual de indicación broncoscópica.

3. Doce (32.4%) tuvieron enfermedad visible endobronchial. En siete se manifestaba por granulomas, en cuatro por deformidades resultantes de la presión ejercida por ganglios linfáticos mediastínicos crecidos, y, enuno por estenosis inflamatoria orificial.

4. Con sólo medicinas se resolvieron los casos de ganglios crecidos y los de membranas mucosas granulosas, pero no los de granulomas ya formados.

5. La extracción broncoscópica de las granulomas y la aspiración del exudado, fueron efectivos en restaurar la apariencia normal de aquellos bronquios visiblemente invadidos por enfermedad granulomatosa.

6. Previamente a la broncoscopía, ni los rayos X, ni los signos clínicos, son datos de confiar en le determinación de cuales niños tendrán enfermedad endobrónquica visible.

7. La broncoscopía es una ayuda importante en el diagnóstico y tratamiento de niños con tuberculosis pulmonar, y debe hacerse en aquellos en quienes el cuadro clínico indica la necesidad de una observación más que meramente casual.

RESUME

1. Les auteurs rapportent une série de 79 bronchoscopies pratiquées sur 37 enfants. Les enfants furent choisis au hasard sans tenir compte des critères habituels qui font décider une bronchoscopie.

2. Douze d'entre eux (32,4%) étaient atteint de lésions endobronchiques visibles. Chez sept, il s'agissait de granulomatose, chez quatre, de déformation due à la compression par des ganglions médiastinaux augmentés de volume et chez un d'entre eux par une sténose orificielle inflammatoire.

3. Par de simples médications, on obtint une résolution des adénopathies médiastinales, et des lésions des muqueuses, mais il n'y eut aucune action sur le granulome constitué.

4. Sa suppression par voie bronchoscopique associée à l'aspiration de l'exsudat, permit de rendre une apparence normal aux bronches, qui étaient de toute évidence atteintes par la maladie granulomatique.

5. Il était impossible de déterminer, soit par l'examen radiologique, soit par l'examen clinique, quel enfant était atteint d'une affection endobronchique. Ce n'est que la bronchoscopie qui le permit.

6. La bronchoscopie est un auxiliaire important dans le diagnostic et le traitement des enfants atteints de tuberculose pulmonaire. On doit y avoir recours chez tous ceux dont le tableau d'ensemble en indique la nécessité, et non pas dans quelques cas isolés.

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Inadequate Tuberculosis Control Within Hospitals

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Tuberculosis case finding among employes in any industry is important for their welfare. The employe found to be afflicted is doubly benefited. His disease can be treated in its early stages before irreparable damage has occurred and the hazard of carrying the infection to his family can be ended promptly. In tuberculosis sanatoriums, as well as in most general hospitals, certain categories of employes are in danger of acquiring tuberculosis either from patients or from material in the laboratories. When so acquired it is occupational tuberculosis. Some hospital employes will develop tuberculosis regardless of their occupation. They acquired the infection before hospital employment and would have developed clinical disease no matter what type of work they did, where they worked or even if they did no work at all. If tuberculosis is found in a hospital employe, the hospital must investigate when and where the infection occurred. Only with detailed knowledge of the occupational hazard can occupational cases be prevented.

Because interns, nurses and other employes of general hospitals have contact with *non-tuberculous* patients it is not only the employes' welfare which requires protection but also the safety of the patients. For their protection, too, the hospital administrator must know that every precaution against spread of tuberculosis within the hospital is effective at all times.

This makes it imperative that every hospital promptly discover active tuberculosis in any of its employes as soon as it becomes demonstrable. If cases are found after they have existed months or years the main objectives of the procedure are lost. Periodic case finding among employes by itself is an important method of tuberculosis control and it is basic to all further steps in control. Without case finding, other measures are useless. From the viewpoint of the patients in a general hospital it is irrelevant whether an employe's tuberculosis is occupational or not. The hazard to the hospital patients is the same.

Ten years ago tuberculosis case finding within hospitals varied from non-existent to complete intensive programs.[1] A few specific cases arising prior to 1942 were published showing failure to discover cases because of insufficient number of examinations.[2] There now are many more institutions which have complete intensive programs and I know of none in which today, case finding among personnel is non-existent. However, there are some hospitals in which case finding is still woefully deficient. Specific instances are here recorded which show an insufficient number of examinations and also serious defects in the case finding technique.

These examples are selected from 200 cases of tuberculosis among hospital employes diagnosed during three years from 1950 to 1953. A

major inadequacy is considered to exist if avoidable delay probably increased the seriousness of the employe's tuberculosis or created for others an unnecessary hazard of infection. I estimate that there is such inadequacy in 20 per cent of employes who become ill. Most nurses training schools have effective case finding; if student nurses are not included in the statistics of hospital employes, the incidence of inadequacies is even higher. These selected cases will demonstrate how and where hospitals have failed.

Failures of hospitals promptly to find tuberculosis among their own employes can be classified in four categories or groups; examples will be cited in each group.

I. Insufficient number of examinations; omission of pre-employment or periodic examinations or both.

II. Periodic chest roentgenograms are done but when a lesion is visible on the film it is missed by the roentgenologist.

III. The roentgenologist reports that he suspects a lesion but his report is filed and no action taken on his findings or recommendations. The employe continues to work in the hospital until the next periodic examination or until he develops symptoms.

VI. Employes who have been exposed resign or retire and do not have a chest roentgenogram at the time of leaving the hospital. Other employes leave when apparently well and are not instructed to have subsequent examinations to determine if they later develop tuberculosis.

REPORT OF CASES

Joseph W. J., employed in 1944 in a general hospital. He helped lift patients and rendered other bedside services. Periodic roentgenograms showed some changes in 1947 and 1948, considered not significant. No further examination until 33 months later when he complained of weight loss, cough and night sweats. Roentgenogram then showed a cavity; the sputum was positive.

Comment: The failure to take periodic x-ray films for 33 months was unfortunate for the employe. It permitted the existence of a tuberculosis hazard for the patients in the hospital.

William D. J., in 1947 employed as a clerk in the admitting room of a large general hospital with tuberculosis wards. He had a history of diabetes for the past 15 years; he was under treatment with insulin and diet. Pre-employment roentgenogram was negative. No further roentgenograms were taken during the four years of his employment.

In 1952 he had a slight hemoptysis. Roentgenogram of the chest showed a moderately advanced tuberculosis, left upper lung. Sputum was positive.

Comment: No periodic examinations for more than four years in an employe who is a known diabetic and is exposed to tuberculosis calls for no comment, only for repentance—and true repentance is to sin no more.

Bertha U. S., employed in the Roentgen ray department for 10 years. She never had a chest roentgen examination until she developed cough and consulted her private physician. Roentgenogram showed advanced tuberculosis with cavity; sputum was positive.

Comment: She now has been ill three and one-half years and the outlook for early recovery is dim. I know of no better nor sadder illustration of the adage: "The shoemaker's children go barefoot."

FIGURE 1

FIGURE 2

FIGURE 3

Figure 1: Dr. Anna X. J. Periodic film of July 1950. The lesion is visible but it was reported negative.—*Figure 2:* Dr. Anna X. J. Periodic film of February 1951. The lesion again is visible but it was reported negative.—*Figure 3:* Dr. Anna X. J. Periodic film of July 1951 correctly reported as showing a cavity.

Dr. Anna X. J., after graduation from medical school in 1949 she served for one year as an intern in Hospital E. Then for one year on the pediatric service of Hospital M. She had had periodic roentgenograms during the two internship years, all of which had been reported as negative.

In July 1951 she was appointed resident physician in pediatrics. A chest roentgenogram made at the beginning of her residency was reported: a 2 cm. cavity in the right upper lung field. Her previous roentgenograms were then reviewed and reported: "Roentgenogram of July 1950 was read as negative but actually reveals a patchy infiltration right first anterior space (Fig. 1). Films of February 1951 and July 1951 reveal further progression" (Figs. 2 and 3).

The lesion can also be seen, though faintly, on the roentgenogram taken more than two years before the diagnosis was made. Roentgenograms in 1949 were negative.

Comment: The roentgenologists failed to see a lesion on two successive periodic films which showed it clearly and on a third on which it was definitely present but faint. As a result, for more than a year she treated children while she had active tuberculosis. Her lesion was untreated and progressed to cavity formation because dual reading of films was not in use.

Joyce T. I. In 1949 employed as an attendant in a general hospital; married, age 18. Chest roentgenogram was normal. Fourteen months later another roentgenogram (Jan. 1951) showed a small density at the right apex but it was missed and the film was reported negative. She was pregnant and was given maternity leave. She was delivered in the same hospital in February 1951. No chest roentgenogram was made while she was in the hospital for this delivery. Four months after her delivery she resumed work in the hospital until August 1951 when she was again pregnant and resigned. In December 1951 she had the second delivery at the same hospital. Again no roentgenogram was taken.

In April 1952 she applied for a position with the telephone company and a preemployment chest roentgenogram showed tuberculosis. She was then admitted to a sanatorium—16 months after the disease was first demonstrable on roentgenograms.

Comment: It is unfortunate for this young woman that her tuberculosis was not found in January 1951 when it was demonstrated on the roentgenogram. She gave birth and took care of an infant after having acquired a fresh, active lesion. During the time that she had an active lesion she continued for some months working in the hospital. Some of the patients, as well as her family and her fellow-employees, were under the hazard of acquiring tuberculosis from this attendant.

Dr. Charles C. P., completed his internship in July, 1950. Periodic roentgenograms, the last one on May 1, 1950, had been reported as negative. Upon completion of his internship he was employed as hospital anesthetist.

September 1951 he had respiratory symptoms. A roentgenogram showed density in the right upper lung area. No other roentgenograms had been taken since May 1, 1950 when he was still an intern. The condition was diagnosed as active tuberculosis and thereupon the roentgenograms made during his internship were reviewed. It was found that the lesion was present on the roentgenogram of May 1, 1950. Roentgenograms prior to May 1950 were negative.

Comment: Because of failure to take periodic roentgenograms during the 14 months of service as an anesthetist and because the lesion had been missed on reading the film of May, 1950, this physician was not put under treatment until 16 months after the tuberculosis was roentgenologically manifest. During these months, as anesthetist, he had more than usual close contact with patients.

Elsie M. S. Nurse in a tuberculosis hospital. Periodic roentgenograms were reported negative until October 1950, when the roentgenologist reported: "increased markings, right upper. Please repeat." No action was taken on this report.

In April 1951 she had another periodic film and the roentgenologist reported: "increased markings, right upper. Suggest lordotic view."

The next film was taken in June 1951 and the roentgenologist reported: "evidence of infiltration in film of October 1950, somewhat larger April 1951 and increased

in extent June 1951." After that the employee was examined and placed under treatment for active tuberculosis.

Comment: The failure is due to the lack of integration of the clinician's and the roentgenologist's share in the case-finding. Nine months elapsed between the roentgenologist's report that further examination was indicated and the time the employee was taken off work and placed under treatment.

John G. P., employed in a tuberculosis hospital in 1946 as an attendant. Pre-employment roentgenogram: No active tuberculosis. Subsequent periodic roentgenograms showed no change until 1951.

Roentgenogram in January 1951 was reported "as far as can be determined reveals no essential change. Examination not entirely satisfactory. Interval study advised." No action was taken on this report.

The next periodic roentgenogram was taken June 1951. The roentgenologist reported: "Infiltration at the level of the third left rib anteriorly." Only after this report was a clinical examination made and treatment for active tuberculosis begun.

Comment: Five months elapsed from the time the roentgenologist recommended "interval study" until the employee was examined, taken off his work and treated.

Margaret H. N., employed in June 1946 at the age of 22 as bacteriology technician in a general hospital. She had graduated from college that same month, having majored in bacteriology. While a college student she had an annual chest roentgenogram.

No pre-employment roentgenogram was taken when she began work. After five months she took 15 weeks sick leave because of pleurisy with effusion. When she resumed work she had no symptom. She continued with her work in the laboratory till July 1949. The work included sputum smears and cultures for tuberculosis and handling of tuberculous pathologic specimens.

In July 1949 she resigned because she was pregnant; her child was born in November. She continued in good health until June 1950, when she developed a cough. A roentgenogram showed a lesion in the left lung. The sputum was positive. Later she had a resection of part of the left upper lobe because of a persistent cavity.

Comment: Her college provided annual chest roentgenograms. After she began work at a hospital where she was exposed to infection, periodic examinations were no longer made! Even after she recovered from pleural effusion, no periodic examinations were made.

It is hazardous to guess for how long before the diagnosis her sputum contained tubercle bacilli. Was it positive while she prepared slides and cultures for the diagnosis of tuberculosis? Though she was an expert technician, if she herself had a positive sputum, were her reports of positive findings of any value or did they lead to gross errors?

Mary C. F., employed as a nurses' aid in a tuberculosis hospital October 1948, at the age of 18. Pre-employment and periodic roentgenograms until December 1949 were negative. In 1949 she was married. In May 1950 she voluntarily resigned. No roentgenogram was taken when she left. No instruction or suggestion was given to her to have a roentgenogram taken in the next few months. In October 1950, because of symptoms, a chest roentgenogram was taken which showed tuberculosis; the sputum was positive. She was admitted as a patient to the institution in which she had worked.

The attending staff physician who reviewed the case for the hospital administration reported "the possibility cannot be discarded that the present disease might have commenced during the last four months of employment."

Comment: If the tuberculosis began as suggested by the staff physician, the omission of an examination on leaving employment was unfortunate for the employe. If the disease developed later it was a serious omission not to instruct her that her hospital exposure made it important for her to have later examinations.

Discussion

Among certain groups in the general population there may be conditions of case finding surveys that make the discovery of most cases of communicable tuberculosis an acceptable program. In hospital personnel surveys, however, the discovery of each and every case is essential.

It is now well known that no individual can read survey chest films without missing a certain percentage of lesions.[3] If films are read by two physicians the error is reduced to almost nil. I have never seen one lesion missed where dual reading is done. Dual reading of films is now routine procedure in many hospital personnel surveys. It should be done in all hospitals. The other errors and omissions in hospital case finding can be remedied by administrative and organizational measures.

The most important step to prevent such gaps in disease control within hospitals and to advance and extend the control is that every institution designate one physician to supervise all phases of tuberculosis control within the institution.[4] He must be competent in tuberculosis epidemiology. He should be responsible directly to the head of the institution. He must investigate, control and eventually eliminate all tuberculosis of occupational origin.[5] He must promptly discover and thus minimize all non-occupational tuberculosis and eliminate the hazard to the hospital patients. The position of epidemiologist must be established permanently in every institution for the sick.

Workmen's Compensation Laws in many states require that the hospital provide necessary care, sick pay and death benefits for any employe disabled by occupational tuberculosis. This is a considerable item in hospital costs. It can be reduced and perhaps eliminated by tuberculosis control based on efficient case finding. The physician's primary concern is with the safety of the hospital patients and the prevention of unnecessary suffering, blighted years and premature deaths of employes. The physician is also concerned because without effective control hospital funds are spent needlessly. Thus, tuberculosis control is not an added expense but an economy measure. Efficient tuberculosis case finding among its employes is a money finding procedure for the hospital.

SUMMARY

Cases are cited of the failure to control tuberculosis among hospital personnel. The failures are due to insufficient examinations and to faulty case-finding technique. This is a health menace to employes and to hospital patients. The remedies are: Case finding to include all hospital employes at all times, improved administration of case finding, dual reading of films and the designation of one physician as hospital epidemiologist to have the responsibility for all aspects of tuberculosis control within the hospital. This control should extend to periodic examination of former employes who have left the hospital where they were exposed to infection.

RESUMEN

Se citan caso en que ha fracasado el control de la tuberculosis entre el personal de hospital. Estas fallas se deben al examen insuficiente y a la deficiente técnica de búsqueda de casos. Esto constituye una amenaza a la salud de los empleados y de los enfermos del hospital. Los remedios son: Investigación de casos que incluya a todos los empleados en todo tiempo, mejor manejo administrativo de esa investigación, doble lectura de las películas y designación de un médico del hospital como epidemiólogo que tenga la responsabilidad de todos los aspectos del control de la tuberculosis dentro del hospital. Este control debe abarcar exámenes periódicos de los antiguos empleados que ya no están en el hospital donde se vieron expuestos a la infección.

RESUME

L'auteur rapporte des cas où l'examen pour tuberculose du personnel hospitalier s'est révélé défaillant. Les erreurs sont dues à des examens insuffisants, et à de mauvaises techniques de recherche. Il y a lá une menace à l'égard de la santé des employés et des malades de l'Hôpital. Pour y remédier, l'auteur propose les solutions suivantes: la recherche des malades doit comprendre tous les employés de l'Hôpital à tout moment. Cette recherche doit être améliorée. Les radiographies doivent être lues par deux personnes et un médecin doit être désigné, avec le titre d'épidémiologiste de l'hôpital, comme responsable de tous les cas suspects de tuberculose lors de l'examen des individus appartenant à l'hôpital. Ce contrôle devrait être étendu et on devrait examiner périodiquement tous les employés, même après qu'ils ont quitté l'hôpital où ils étaient exposés à l'infection.

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The Treatment of Pulmonary Blastomycosis*

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Blastomycosis is considered the rarest and most lethal of the three common pulmonary mycotic infections. In the United States these diseases have a fairly well fixed geographical distribution.[1] Coccidioidomycosis is confined largely to the southwestern states and histoplasmosis to the Mississippi Valley and the St. Lawrence River area. Since North Carolina occupies the center of the endemic area for the North American type of blastomycosis, it is not surprising that 13 patients with pulmonary involvement and two with cutaneous manifestations of the disease have been seen at Oteen during the past 10 years. One of the latter patients also had pulmonary involvement. Two of these cases have been reported previously.[2] We are now reporting our total experience, with the group of patients with pulmonary involvement, in the hope that the collected experiences of several centers will result in the development of a more effective plan of management than has heretofore been available. A summary of the clinical and pathologic findings, the treatment and results of treatment in our 13 cases is presented in Table I. Following infection with the causative agent, a double-contoured, single-budding yeast-like organism, two clinical forms of the disease are recognized.[3, 4] Cutaneous blastomycosis occurs in about half the cases, usually, it is thought, as a result of dissemination of a recognized or unrecognized primary pulmonary focus.[5] Primary cutaneous inoculation blastomycosis, however, does occasionally occur. The respiratory tract is thought to be the portal of entry for the systemic type in which the lungs, bones,[13] and lower genito-urinary tract[15] are most commonly involved. In many patients, of course, both skin and visceral manifestations are present.

Pathology

The pathologic lesion produced by blastomycosis is a chronic granuloma which at times is indistinguishable from those of tuberculous origin.[3, 4] Micro-abscess formation, however, with polymorphonuclear and giant cell components is a characteristic which should arouse suspicion. Definite diagnosis depends upon the demonstration of blastomyces dermatitidis either histologically or bacteriologically and preferably by both methods.[6, 7] Micro-abscess formation was noted in all except one of our patients in

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whom material was available for histological study. The single exception was in a white male who had received intensive treatment with undecylenic acid for nearly five months prior to lobectomy for a 2½ centimeter cavity. Only one organism was seen in the cavity wall. Culture from this lesion was positive. Blastomyces dermatitidis was seen or cultured from the tissues in every case in which pathologic material was available to us.

Martin and Smith[3, 4] reviewed the literature in 1939 and found that cavities larger than one centimeter in diameter were rarely seen. Schwarz

SUMMARY OF THIRTEEN CASES OF SYSTEMIC NORTH AMERICAN BLASTOMYCOSIS[1]

Case No.	Age	Race	Occupation	Symptoms at Onset	Sputum	Blastomycin Skin Test	Complement Fixation	Bronchoscopy
1	55	N	Farmer	Productive cough	—	Not done	Not done	Evidence of old endobronchial disease
2	31	W	Textile worker	Productive cough, chest pain	+	Not done	Not done	No pathology
3	36	W	Laborer in lumber mill	Chest pain hemoptysis	+	+	—	None recorded
4	27	N	Farmer	Chest pain	+	—	+	Endobronchial hyperemia
5	31	W	Textile worker	Hemoptysis, productive cough	+	+	Not done	Small ulcer, RUL orifice. Tenacious white secretions RML orifice
6	34	N	Steel construction laborer	Hemoptysis, chest pain	+	+	+	Negative
7	40	W	Watchmaker, farmer	Chest pain	—	+	—	Small amount purulent secretions LUL orifice

[1]All patients were males.
[2]Blastomyces dermatitidis identified on histopathological examination or cultured from specimen.
[3]No tissue available for study.

and Baum,[5] after a study of 58 reported cases in 1951, found no definite cavities. Two of Feld and Cadden's 11 cases,[8] two of Weisel and Landis' seven cases,[9] and six of our 13 cases, however, had cavities up to seven centimeters in diameter shown on the chest film. In four of the seven cases in which pathologic material from the lung was available to us, cavities ranging from less than one centimeter to 2½ centimeters in diameter were found. Baker[10] states that cavities frequently develop in lungs which are the site of chronic pulmonary blastomycosis.

SUMMARY OF THIRTEEN CASES OF SYSTEMIC NORTH AMERICAN BLASTOMYCOSIS[1]

	PATHOLOGY			TREATMENT				
Diagnosis Made On	Cavity	Micro-abscesses	Organisms in Tissue[2]	Surgery	Potassium Iodide	Undecylenic Acid	Stilbamidine	Remarks
Biopsy and culture of skin	3 cm.	+	+	—	+	—	—	Pulmonary lesion not proven to be due to blastomycosis. Died in 1948. Had sputum positive for acid-fast organisms at death. Histology consistent with blastomycosis.
Culture Positive Sputum, skin pustule, blood	None	+	+	—	+	—	—	Died in 1946. Resection recommended but dissemination occurred before surgery could be done.
Sputum	2.5 cm.	?[3]	?[3]	+[3]	+	+	+	Chronic recurrent pneumothorax for 14 years prior to diagnosis of blastomycosis. Decortication and excision of wall of abscess done elsewhere. Clinically well but sputum remains positive. Followed 5 years since diagnosis. February 1954 sputum also positive for acid-fast bacilli. Severe trigeminal neuropathy. Remains positive (sputum) after a 15 gram course of 2-hydroxystilbamidine.
Rib biopsy, sputum, pus from chest wall abscess	None	+	+	+	+	—	—	Rib resection and incision and drainage of abscess. Died in 1948. Autopsy
Sputum	2.0 cm.	?[3]	?[3]	—	+	—	—	Clinically well except for recurrent hemoptyses. Followed by letter 3 years since onset. Sputum positive for blastomyces dermatitidis 5-11-54.
Sputum and surgical specimen	Less than 1.0 cm.	+	+	+	+	—	—	Died of disseminated disease six months after pneumonectomy. Autopsy.
Surgical specimen, pleural fluid and skin pustules	None	+	+	+	+	+	—	Clinically well following pneumonectomy and undecylenic acid. Followed 2½ years since surgery, sputum remains negative, X-rays clear.

Clinical Findings

The disease occurs most frequently in young adult males. All of our patients were males. One-third were Negroes. This is consistent with the report of Martin as to racial distribution.

No characteristic clinical syndrome presents itself. The onset in the majority of our patients was characterized by productive cough. Chest pain occurred in six, and hemoptysis in five. A history of spontaneous pneumothorax was given by two patients. One other was admitted with symptoms referable to the genito-urinary tract. This case has been reported in detail elsewhere.[11] The diagnosis was made on study of the

SUMMARY OF THIRTEEN CASES OF SYSTEMIC NORTH AMERICAN BLASTOMYCOSIS[1]

Case No.	Age	Race	Occupation	Symptoms at Onset	Sputum	Blastomycin Skin Test	Complement Fixation	Bronchoscopy
8	34	W	Weaver, house painter	Hemoptysis	+	—	—	Slight endobronchial hyperemia
9	25	W	Farmer	Hemoptysis, chest pain	+	—	—	Hyperemia and purulent secretions RUL orifice
10	24	W	Clerk	Cough, chest pain	+	—	—	Hyperemia Rt. main bronchus; thick mucopurulent secretions RUL orifice
11	55	W	Carpenter	Perineal pain, weak urinary stream	—	—	+	Not done
12	38	N	Laborer in mill	Productive cough	+	—	—	Negative
13	60	W	Railroad man	Chronic cough, dyspnea	+	—	—	Edema and hyperemia RUL orifice

[1]All patients were males.
[2]Blastomyces dermatitidis identified on histopathological examination or cultured from specimen.
[3]No tissue available for study.

sputum in nine, by biopsy of skin, bone, or from the surgically resected specimen of lung in four, and from the study of the prostatic smear in one. Skin tests for blastomycosis were negative in seven, positive in four, and not done in two. Complement fixation was also negative in seven, positive in three and not done in three others.

Bronchoscopic examination revealed either no abnormality of the tracheobronchial tree or non-specific hyperemia with purulent secretions in most of our cases. Ulceration of the bronchial mucosa was seen only once. This is in contrast to the bronchoscopic findings of Weisel and Landis,[9] who reported mucosal ulceration with brown secretion in the tracheobronchial tree as a characteristic of the disease in their seven patients.

SUMMARY OF THIRTEEN CASES OF SYSTEMIC NORTH AMERICAN BLASTOMYCOSIS[1]

	PATHOLOGY			TREATMENT				
Diagnosis Made On	Cavity	Micro-abscesses	Organisms in Tissue[2]	Surgery	Potassium Iodide	Undecylenic Acid	Stilbamidine	Remarks
Sputum and surgical specimen	2.5 cm.	—	+	+	—	+	—	Right lower lobectomy after preparation with undecylenic acid. Clinically well 17 months since surgery. One positive smear of sputum 11 months after surgery, unconfirmed by subsequent smears and cultures. Negative 8-(26-27-28)-53.
Sputum	None	?[3]	?[3]	—	—	+	—	Treated with undecylenic acid alone. Clinically well with sputum negative for 18 months since treatment stopped. X-rays now negative.
Sputum, surgical specimen	2.5 cm.	+	+	+	—	+	+	Right upper lobectomy, followed by undecylenic acid and stilbamidine for ipsilateral spread. Clinically well but sputum remains positive 22 months after surgery. Severe trigeminal neuropathy. Recently given 8 grams of 2-hydroxystilbamidine.
Skin and pus from prostatic abscess	None	+	+	+	+	+	+	Disease apparently arrested after I & D of prostatic abscess, and bilateral orchiectomy and epididymectomy. Residual weakness left arm and leg. Discharged from hospital 9-17-52 and remains well. Severe trigeminal neuropathy.
Sputum	5.0 cm.	?[3]	?[3]	—	—	—	—	Cavitary lesion on X-rays of chest present for 10 years. Patient left hospital against advice, untreated.
Sputum, bronchoscopic washings	None	?[3]	?[3]	—	—	+	+	Clinically well with sputum negative and roentgenographic clearing. Treated with undecylenic acid and stilbamidine concomitantly. Sputum cultures negative six months after discharge. Has moderate trigeminal neuropathy.

Treatment and Results

Eight patients were treated with potassium iodide alone, or in conjunction with some other type of medical or surgical care. When indicated by the blastomycin skin test, desensitization was carried out prior to initiation of treatment. Three patients received iodides as the only method of treatment. One of the a patient with blastomycosis of the skin, in addition to bilateral pulmonary infiltration, left the hospital against advice in 1945 and died in 1948. Prior to death, acid-fast bacilli were present in the sputum although the chest x-ray film showed no significant change since 1945. At autopsy blastomyces dermatitidis were readily demonstrated in the skin lesions. Neither tubercle bacilli or fungi were found in the histological sections of the lungs. The microscopic picture, however, was consistent with blastomycosis. One patient died following systemic dissemination, a month after admission, and one is clinically well but has an occasional hemoptysis, residual bronchiectasis, and sputum which contains blastomyces dermatitidis three years after the orginal admission.

Five patients were given iodides in conjunction with some form of surgery. Decortication was carried out in one, pneumonectomy in two, drainage of a prostatic abscess in one, and rib resection with drainage of a lung abscess in one. Two of these five are dead, one recovered after a post-pneumonectomy systemic dissemination was treated with undecylenic acid, and two required subsequent treatment with other agents.

In summary: Iodides were used either alone or in conjunction with other forms of therapy in eight patients. Four of whom are known to be dead, two have recovered after discontinuing iodides and using other agents and two remain clinically well but carry the organisms in the sputum. Potassium iodide therapy has not been a satisfactory method of treatment in our hands.

Undecylenic Acid

Undecylenic acid* was given to seven patients, two of whom had been treated originally with iodides. The initial dose was five grams per day, orally. This was rapidly increased to a maintenance dose of 10 to 25 grams daily. Sixty-one (61) grams a day were tolerated by the last patient treated, without any toxic manifestation. The average duration of treatment was 40 weeks. The average total dose of the drug used was 4596 grams. Some of these patients received, in addition, 600 mg. of ascorbic acid daily and 12 mg. of Vitamin K.

In one patient undecylenic acid was the only agent used. He had a pneumonic infiltration in the right upper lobe which resolved completely. A systemic dissemination which followed pneumonectomy for a supposed carcinoma in another patient was cured after an initial failure with iodides. One patient who had a 2½ centimeter lower lobe cavity and repeated hemoptyses, was prepared for resection with a three months' course of undecylenic acid. He has recovered and is working. One patient with chronic bilateral cavities had decortication and excision of a 2½

*Obtained from Bio-Products Company, Warrenton, Oregon.

centimeter cavity three years before admission. He remains clinically well although his sputum continues to show organisms in spite of treatment with iodides, undecylenic acid, stilbamidine and dihydroxystilbamidine. Acid-fast organisms have also been found in his sputum recently. One patient had upper lobectomy for chronic abscess and a diagnosis of blastomycosis was established in the tissue section. He was treated postoperatively with undecylenic acid but developed a new lesion in the ipsilateral superior segment. The x-ray shadow lesion cleared under stilbamidine treatment but the sputum continues to be positive. One had a systemic dissemination from a prostatic abscess which improved after drainage and undecylenic acid treatment but complete recovery was not made until stilbamidine was administered. The last patient was treated with undecylenic acid and stilbamidine concomitantly for a pneumonic lesion of the upper lobe which cleared completely. The sputum also became negative under treatment.

Thus, it can be said that there was clear-cut evidence of the value of undecylenic acid in two patients and strongly presumptive evidence in two others. In three clinical improvement occurred but curative results were not obtained.

Stilbamidine

Stilbamidine was given to four patients intravenously in doses of 150 mg. per day, after testing for reaction to smaller doses. An average of 6.8 grams of the drug were given in two or three courses. Three of these patients represented failures with other methods of treatment. One had been given decortication, iodides, and undecylenic acid. One had lobectomy followed by undecylenic acid treatment and one had drainage of a prostatic abscess followed by iodides and undecylenic acid. The fourth was treated with undecylenic acid and stilbamidine concomitantly for a pneumonic lesion. Three of them had positive sputum before treatment was begun. It remained positive in two, following treatment with stilbamidine. Marked clinical improvement was noted in two and some degree of improvement in all four.

There is rather definite evidence that stilbamidine was a lifesaving agent in the patient with systemic dissemination from the prostatic abscess. It was of presumptive value in the patient treated concomitantly with undecylenic acid. From a curative aspect it was a failure in the remaining two patients. Trigeminal neuropathy of a severe degree developed in all four of these patients, however. In evaluating the drug it must be noted that the patients who were considered failures had also resisted treatment with other available agents. 2-hydroxystilbamidine was also given to two of these patients after failure with stilbamidine. In one the sputum culture remained positive after a course of 15 grams of 2-hydroxystilbamidine. The second patient received 8.0 grams of the drug. Negative sputum smears have been obtained from this patient but the cultures are unreported.

TABLE II
PULMONARY RESECTION FOR BLASTOMYCOSIS

No.	Author	Year	Author's Case No.	Pathology	Type of Operation	Follow-up	Result	Remarks
1	Feld and Cadden	1947	11	Not stated	Lobectomy	—	Died	Dissemination with spread to opposite lung and various parts of body.
2	Lowry, et al	1951	1	Solid granuloma with micro-abscess formation	Right lower lobectomy	8 mo.	Good	Pre-op. diagnosis was "cyst" of the lung. No evidence of residual disease post-op.
3	Good, et al	1951	—	Chronic granuloma	Resection		Good	
4	Buechner, et al	1953	1	Solid circumscribed granuloma	Right lower lobectomy	9 mo.	Good	Uneventful convalescence on bed rest alone.
5	Buechner, et al		2	Granuloma with necrosis	Right upper lobectomy	19 mo.	Good	"Reactivation" post-op. in right lung, responded to KI, blastomycin, and human serum.
6	Weisel and Landis	1953	3	Abscess cavity	Decortication followed by right middle and lower lobectomy	16 mo.	Good	Uneventful convalescence.
7	Weisel and Landis		5	Abscess cavity	Right lower lobectomy	12 mo.	Good	Uneventful convalescence. Apical pneumothorax space for 4 mos.
8	Cummins, et al	1953	1	Chronic pneumonitis	Right upper lobectomy	3 mo.	Good	Skin lesions appeared 12 months after operation, cleared up with KI and stilbamidine.
9	Smith, D. T.	1953	4	Not stated	Right upper lobectomy	5 mo.	Good	Stilbamidine given following operation.
10	Takaro, et al	1954	6	Pneumonia, micro-abscess and "pseudo-tubercles"	Right pneumonectomy	—	Died	Spread to opposite lung, with death 6 months after operation.
11	Takaro, et al		7	Chronic granuloma	Left pneumonectomy	30 mo.	Good	Skin lesions appeared 4 months after surgery, responded to undecylenic acid, but not to KI.

12	Takaro, et al		8	Chronic cavitary disease	Right lower lobectomy	17 mo.	Good	Undecylenic acid pre- and post-op. One positive sputum 11 months post-op., unconfirmed by subsequent cultures.
13	Takaro, et al		10	Cavitary and micro-abscess formation	Right upper lobectomy	10 mo.	Fair	Residual disease in right lower lobe increased on roentgenograms, but has regressed on undecylenic acid and stilbamidine therapy, although sputum remains positive.
14	DeCamp, et al	1954	1	Not stated	Left pneumonectomy	32 mo.	Died	Post-op. bone metastasis. Died of cardiac arrest during rhizotomy. Diagnosis established post-op.
15	DeCamp, et al	1954	2	Not stated	Right pneumonectomy	69 mo.	Good	One post-op. sputum positive. All others negative. Diagnosis established post-op.
16	DeCamp, et al	1954	3	Cavity 4 cm. in diameter	Left upper lobectomy	66 mo.	Good	A persistent cavitary lesion apparently cured by lobectomy. Diagnosis established post-op.
17	DeCamp, et al	1954	4	Chronic granuloma	Right upper lobectomy	5 mo.	Died	Death occurred 5 months post-op. of coronary thrombosis. Diagnosis of blastomycosis made post-op.
18	DeCamp, et al	1954	5	Chronic granuloma	Left upper lobectomy	—	Died	Sinus tachycardia during surgery. Died 3 hours post-op. Autopsy revealed pheochromocytoma of the left adrenal. Diagnosis of blastomycosis made post-op.
19	DeCamp, et al	1954	6	Cavitary lesion; fibrosis	Left lower lobectomy	8 mo.	Good	Three pre-op. courses of 2-hydroxystilbamidine (Total 9.0 grams) prior to resection for a systemic disseminated lesion.
20	Hughes, et al	1954	2	Chronic granuloma miliary abscesses	Right lower lobectomy	29 mo.	Good	Diagnosis established post-op.
21	Hughes, et al	1954	3	Multiple small granulomata with caseous necrosis and fibrosis	Left upper lobectomy	14 mo.	Good	Preoperative iodide treatment.
22	Sealy, et al	1954	1	Extensive lung destruction	Left upper lobectomy	21 mo.	Good	Preoperative iodide therapy. Postoperative desensitization and iodides for contralateral spread.
23	Sealy, et al	1954	2	Marked destructive changes consistent with blastomycosis	Right pneumonectomy	18 mo.	Good	Pre- and postoperative desensitization with blastomyces vaccine.

Surgical Treatment

Surgical treatment was used as an adjunct in seven patients. Pulmonary resection was carried out in four patients, two pneumonectomies and two lobectomies. Decortication of the lung and unroofing of an abscess pocket was done in one, bilateral epididymectomy and orchiectomy in one, and excision of a rib and drainage of a lung abscess in one. One pneumonectomy was done for an acute pneumonic involvement of the entire right lung. Contralateral involvement was probably present but not recognized prior to surgery. After pneumonectomy there was a gradual increase in disease in the remaining lung and he succumbed six months after resection in spite of iodide therapy. Neither undecylenic acid nor the diamidines was then available. The other three patients who had resections were described with the undecylenic acid group. They are all clinically well although one still harbors the fungus organism in the sputum. Those surviving resection, however, had lesions of a more chronic type. The diagnosis of blastomycosis was made postoperatively in two of the three.

Discussion

The use of potassium iodide has been a time-honored method of treatment for fungus infection of the lung.[3, 4] Although scattered reports of favorable results[8, 9, 12, 16] continue to appear in the literature, the overall results have been discouraging. A multiplicity of other types of treatment[9, 10, 12, 16, 18, 19, 21, 23] such as curettement, drainage of abscesses, roentgen therapy, the use of gentian violet and of colloidal copper sulfate have also been disappointing.[12] McVay and Carroll reported the successful use of aureomycin in two patients in 1952. It appears, however, that treatment must be continued indefinitely.[17] Results following the use of aureomycin were reported to be poor by other workers.[10, 18, 19] Other antibiotic and chemotherapeutic agents, including the sulfonamides, penicillin, streptomycin, terramycin, and chloromycetin have also been ineffective.[9, 19, 16, 18, 23] Ethyl vanillate has been given a trial;[12] cortisone has also been used several times.[19, 21] Neither seemed to be of significant value. Diethylstilbestrol, however, when given for prostatic carcinoma to two patients, brought about a regression of the cutaneous lesions of blastomycosis, according to Curtis and his co-workers, and might be worthy of further trial.[21]

Recently, three new methods of treatment have been advocated; namely, the use of resective surgery, of stilbamidine or 2-hydroxystilbamidine given intravenously, and undecylenic acid by mouth.

The earliest report of pulmonary resection for blastomycosis which we could find was that of Feld and Cadden (Case 11).[8] This patient died of disseminated disease following treatment with potassium iodide and lobectomy. We have collected reports on 23 patients[31, 32, 33] (Table II), including four of our own, who have had some type of pulmonary resection. The diagnosis was established postoperatively in at least 10 of the 23. Five died. Six cases with insufficient data for analysis, referred to by Baker, are not included.[6, 9, 14, 19, 24, 25, 26] The usefulness of surgery without ad-

TABLE III
TREATMENT OF BLASTOMYCOSIS WITH STILBAMIDINE[1]

No.	Author	Year	Author's Case No.	Clinical Form of Disease	X-Ray Evidence of Pulmonary Involvement	Sputum Pos. for B. Dermatitidis	Toxic Neuropathy	Length of Follow-up in Months	Result
1	Schoenbach, et al	1952	1	Systemic	+	?	+	6	Good[2]
2			2	Systemic	+	?	+	5	Good
3			3	Systemic	?	?	—	0	Good
4			4	Systemic	?	?	+	0	Improved[3]
5	Baker, et al	1952	1*	Cutaneous	?	?	—	?	Good
6			2*	Systemic	?	?	—	?	Good
7			3*	Systemic	?	?	+	?	Good
8	Curtis, et al	1952	3	Systemic	+	+	—	4	Good
9			4	Systemic	+	+	—	0	Good
10	Cummins, et al	1953	1	Systemic	+	—	+	0[4]	Good
11			2	Systemic	+	—	+	6	Good
12	Pariser, et al	1953	1	Systemic	+	+	—	13	Good
13	Black, et al	1953	1	Systemic	+	+	+	16	Good
14	Levitas, et al	1953	3	Systemic	+	+[5]	Died	—	Died
15	Stillian	1953	1	Cutaneous	?	?	+		Good
16	Thorgerson	1953	1	Systemic	+	+	—	?	Improved[6]
17	Smith, D. T.	1953	1	Systemic	?	?	+	14	Good
18	Smith, D. T.	1953	2	Systemic	+	+	+	9	Good
19	Smith, D. T.	1953	3	Systemic	+	+	+	9	Good
20	Smith, D. T.	1953	4	Systemic	+	?	+	5	Good
21	Smith, D. T.	1953	5	Systemic	?	?	+	4	Good
22	Smith, D. T.	1953	6	Systemic	?	?	+	5	Good
23	Smith, D. T.	1953	7	Systemic	+	?	+	4	Good
24	Smith, D. T.	1953	8	Cutaneous?	?	?	?	4	Good
25	Smith, D. T.	1953	9	Systemic	+	?	—	3	Good
26	Smith, D. T.	1953	10	Cutaneous?	?	?	?	4	Relapsed
27	Takaro, et al	1953	3	Systemic	+	+	+	4	No Change[7]
28	Takaro, et al	1953	10	Systemic	+	+	+	4	Improved[8]
29	Takaro, et al	1953	11	Systemic	+	—	+	8	Good
30	Takaro, et al	1953	13	Systemic	+	+	+	0[9]	Good

Code: + Positive or yes
— Negative or no
? Unknown or unreported

[1]Five patients had excisional surgery in addition: Case Numbers 3, 10, 11, 18 and 19
[2]Residual esophageal stricture
[3]B. dermatitidis cultured after treatment
[4]Treatment continuing
[5]Bronchoscopic aspirate
[6]Draining sinus and pulmonary infiltrate remain

*Mentioned only in addendum to paper

junctive drug therapy is a questionable method of treatment.

Colbert and others are credited with the earliest report of the use of one of the diamidines (propamidine) for cutaneous blastomycosis.[27] Schoenbach and his associates, on the other hand, were first to report the successful use of stilbamidine in 1951 in the treatment of systemic blastomycosis in a patient with mediastinitis following perforation of the esophagus by a bougie.[28] Including this early success, reports of 26 patients with cutaneous or systemic blastomycosis, or both, treated with stilbamidine (as well as other agents) have appeared in the literature.[10, 12, 18, 20, 22, 23, 26, 29] To this series we are adding four of our own (Table III). Twenty-six of these 30 cases were the systemic form and 19 had definite roentgenographic evidence of pulmonary involvement. The sputum was reported positive for the fungi in only 11 of the 30 cases before beginning treatment. Good results were achieved in 25, with an average follow-up of about five months. There was no change in one, residual disease remained in several and blastomyces dermatitidis was cultured in three cases after treatment. One died, after a week of intravenous stilbamidine, of diffuse hepatic necrosis and generalized blastomycosis.[12] The characteristic trigeminal neuropathy, peculiar to the use of this drug was reported to have occurred in 18 of the 30 cases in which it was used. Snapper's recent work suggests a more extensive trial of 2-hydroxystilbamidine, which is believed to be about as effective as stilbamidine against blastomyces dermatitidis but does not produce the toxic neuropathy noted so frequently with stilbamidine.[30]

The use of undecylenic acid for pulmonary blastomycosis was first reported by two of us in 1952.[2] Since then, although no other reports of its use have yet appeared in the literature, it has been given to at least seven additional patients of whom we have knowledge. No toxic effects of undecylenic acid were observed in any patient and none has died. Without doubt, a longer follow-up period will be necessary before the exact place of any of these three methods of treatment—resection, the use of undecylenic acid, or of the diamidines, in the treatment of blastomycosis can be determined. It may be that the combination of 2-hydroxystilbamidine and undecylenic acid will prove to be the most effective means of treatment. However, even when stilbamidine, undecylenic acid, and resective surgery were all used in two cases, the sputum remained positive for blastomyces dermatitidis and roentgenographic evidence of residual disease persisted, although both were clinically well.

Conclusions

From this study, one can only conclude that a completely satisfactory form of treatment for pulmonary blastomycosis has not yet been found. Pulmonary resection for localized, stable lesions after immunological balance is obtained may be an important therapeutic aid. The use of undecylenic acid orally and of stilbamidine or 2-hydroxystilbamidine intravenously are useful measures. Combined therapy with undecylenic acid and one of the diamidines may be the best method of drug treatment

available.

(We wish to acknowledge the technical assistance of our mycologist, Mr. Carl J. Hogue).

Addendum

Our attention has been brought to still another case of blastomycosis treated successfully with undecylenic acid. This is the case of Dr. Pinto of the Fayetteville Veterans Administration Hospital. A 32-year-old white male was found to have osteomyelitis of the 11th rib, left, from which blastomyces dermatitidis was cultured. He was treated with undecylenic acid for 10 weeks with regeneration of a destructive lesion in this rib and healing of a draining sinus in the same area of eight months duration.

SUMARIO

Se concluye de este estudio que todavía no ha sido encontrado un tratamiento completamente satisfactorio para la blastomicosis pulmonar. La resección pulmonar puede ser una importante ayuda terapéutica para lesiones localizadas estables después de obtenido el balance inmunológico. Es de utilidad el uso oral del ácido undecilénico y de la estilbamidina o 2-hidroxiestilbamidina intravenosa. Es posible que el tratamiento combinado de ácido undecilénico y una de las diamidinas, sea el mejor método disponible en el tratamiento medicamentoso.

RESUME

A la suite de l'étude faite par les auteurs, on peut simplement conclure que jusqu'à présent, il n'a pas été découvert de traitement tout à fait satisfaisant pour la blastomycose pulmonaire. Des exérèses pulmonaires pour des lésions localisées stables après que l'élément infectieux ait pu être diminué, peuvent être d'un secours thérapeutique important. L'utilisation par voie buccale de l'acide undécylénique et de la stilbamidine (2-hydroxystilbamidine) par voie intra-veineuse est un procédé utile. Un traitement combiné avec l'acide undécylénique et l'une des diamidines est peut-être la meilleure médication actuellement à notre disposition.

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Resectable Bronchogenic Carcinoma
A Study of 120 Cases

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This work is based on 120 resected cases of cancer of the lung. The patients came from Hospital Nacional de Clínicas, Buenos Aires, Argentina, and from the medical group "Clínica del Tórax." I am very much obliged to its members. The main purpose of this study was to find the symptomatology, if any, of cancer of the lung susceptible of resection.

We looked for differentiating characteristics, pathognomonic signs or any other clinical factor that would permit us to say: "In this particular case of cancer lung resection of the lesion will be possible, because those certain factors are present." We studied the histories of the 120 patients that underwent successful resections. We analyzed the age, sex and clinical onset syndrome, the time that elapsed from the clinical onset until the diagnosis was made, and the radiologic, bronchoscopic and pathologic findings.

We must say at the outset that, at the beginning, cancer of the lung has no malignant characteristics. It seems just like some harmless condition of the respiratory tract. When the malignant picture appears it is too late and there is no hope of cure. The cancer susceptible of resection is that one which, from the clinical point of view, never appears like a typical cancer.

Age:

In our statistical series of 120 resected cases the most common age was between 41 and 60 years; 86 cases (71.6 per cent) belong in this group. In this 20-year age period (41-60) there was some variation in incidence according to the histological type of cancer. The undifferentiated carcinomas had their peak between 41 and 50 years of age (10 in 22 cases, 45.4 per cent), there were only three cases between 51 and 60 years, but five between 31 and 40 and one under 30 years of age. The undifferentiated prefers young people. The other two types of carcinoma, adenocarcinoma and epidermoid, appear in older people.

The adenocarcinomas, with a total number of 44, occurred in 20 cases between 41 and 50 years and in 13 between 51 and 60. Undoubtedly the epidermoid prefers older people than the adenocarcinoma. There were 54 epidermoids resected. Of these, 16 were in patients between 41 and 50 years and 23 in others between 51 and 60 years. There were also eight between 61 and 70 and one over 70 years of age. (There was also one resected adenocarcinoma in a patient over 70 but no undifferentiated carcinoma in this age period.) No adenocarcinoma or epidermoid appeared under 30 years of age. Our series is completely different from that of Ochsner's.[1]

Sex:

All authors agree with the fact that, without any reasonable explanation, cancer of the lung predominates in men over women. In Ochsner's series,

among 190 cases 27 were women (14.2 per cent) and 50 per cent of their cancers were adenocarcinomas. In our 120 resected cases only one was a woman (0.83 per cent). Undoubtedly, adenocarcinoma is the most common feminine cancer of the lung. Our only case was an adenocarcinoma (Case 40). We do not know the reasons why in Argentina cancer of the lung in women is so extremely rare. (Less smoking than in the U. S. A.?)

Onset Syndromes:

We have written elsewhere that cancer of the lung progresses slowly, begins without any malignant characteristic and simulates some trivial respiratory disease.[2] When the classical picture of malignancy appears, it is because complications already exist, the cancer has propagated or metastases have occurred. In other words, when we see a patient with the classical symptomatology of cancer of the lung, there is no hope of cure.

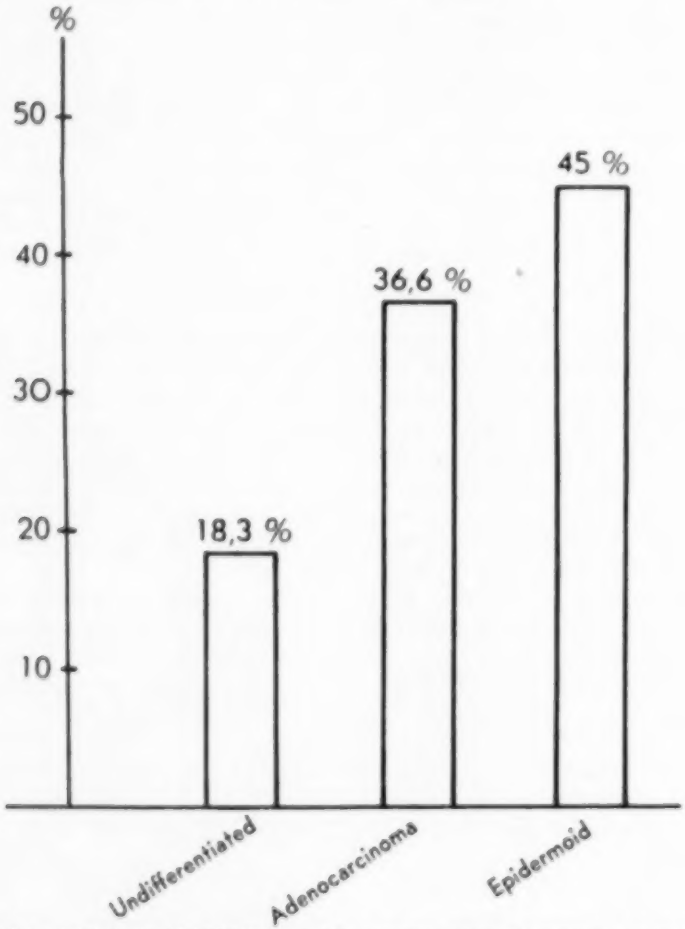

FIGURE 1: Histologic distribution of 120 resected cases of cancer of the lung (all cases).

The cancer susceptible of resection has an initial symptomatology which is absolutely innocent. We call this the "useful" period of cancer which can be encountered only by means of early diagnosis.

The clinical and pathological picture presents no pathognomonic signs or syndromes. With these fundamental facts in mind we propose the adoption of a simple clinical policy: the routine suspicion of cancer.

The physiopathology of cancer of the lung explains the three principal causes of its symptoms and signs:

1) Bronchial obstruction.
2) Ulceration and infection.
3) Extrathoracic symptoms (endocrine?).

These three physiopathological mechanisms intermingle their signs and symptoms as the cancer grows and so, in the "status" period, it is difficult to differentiate one from the other.

Our 120 resected cases of cancer of the lung presented the following onset syndromes:

			Per Cent
I Without symptoms (discovered by health examination)			3.3
II With Symptoms	1) Bronchial Syndrome 51.6 percent	Catarrhal	13.3
		Haemoptic	28.3
		Painful	10.0
	2) Bronchial Syndrome with Pneumonitis		15.0
	3) Thoracic pain Syndrome		9.1
	4) Extrathoracic Syndromes 20.7 percent	Rheumatoid	18.3
		General debility	0.8
		Febrile	1.6

We believe that at present the best way to combat cancer is by its early diagnosis through a complete health examination. The success of this procedure is based upon the fact that when the physician discovers cancer in this manner the disease is still without symptoms because as yet no spread

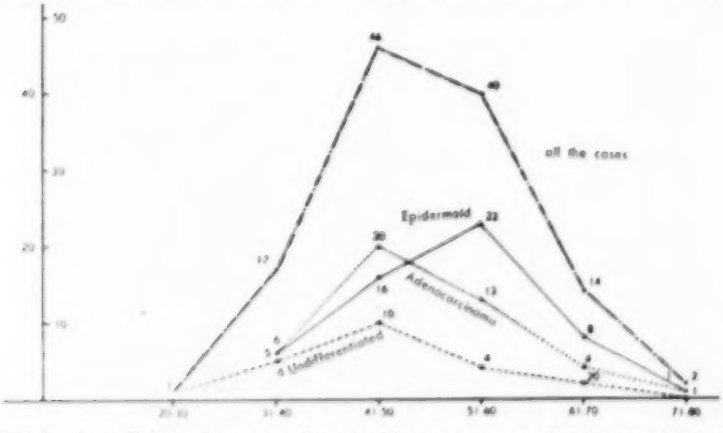

FIGURE 2: Age distribution according to histologic type of 120 resected cases of cancer of the lung.

or complications have occurred. In our series four were discovered by health examinations (two adenocarcinomas and two undifferentiated, 3.3 per cent of the total.) It is true, though, that it is difficult to convince people who do not have respiratory symptoms, not even cough, to undergo such a major operation as pulmonary resection.

If we keep in mind that carcinoma of the lung is bronchogenic, it is easy to understand why the most important onset syndrome is related to bronchial irritation. Half of the resected cases in this series (51.6 per cent) began with bronchial symptomatology: catarrh, cough, hemoptysis.

(1) Hemoptoic sputum is more common than frank hemoptysis as an onset sign. In 28.3 per cent of the resected cases hemoptysis or hemoptoic sputum was present as the onset syndrome. The hemoptoic is important from the point of view early diagnosis because this symptom, blood in the sputum, makes such a strong impression on the patient that he goes almost immediately to the physician. Luckily, hemoptysis is always followed by a chest x-ray film. Thirty-four resected cases in our series began in this manner (eight undifferentiated, 10 adenocarcinomas and 16 epidermoids.)

Many authors have denied the existence of the bronchial and painful form as an onset syndrome. In our series we encountered 12 cases of this nature (10.0 per cent). This is not the classical pain of invading cancer: continuous, radiating along the distribution of the invaded nerves. In our cases the pain was of sympathetic origin: deep, without exact localization. Perhaps one could look for its actual cause in atelectasis or infection.

(2) Many cases began with a picture of pulmonary infection, with cough, mucopurulent expectoration, fever, debility, loss of weight, etc. In order of frequency this is the third most common onset syndrome and we have named it bronchial syndrome with pneumonitis (15 per cent of the total cases.) Accordingly we can say that in patients over 40 years of age in whom the proper use of antibiotics does not resolve their bronchopulmonary disease in a reasonable length of time, the x-ray film will show that, in many instances, the real cause of pneumonitis or unresolved pneumonias is cancer of the lung. The reason is that the antibiotics attack

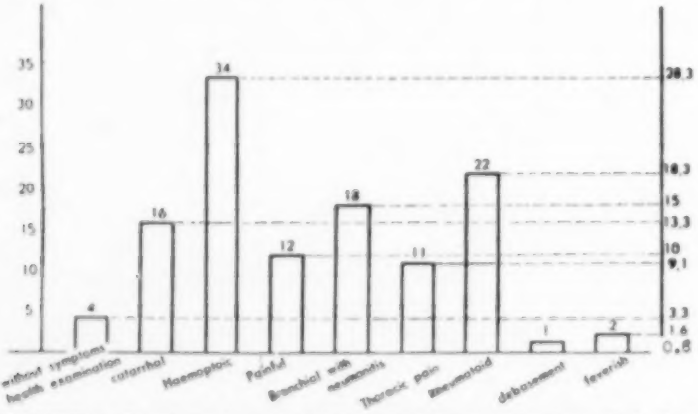

FIGURE 3: Onset syndromes of 120 resected cases of cancer of the lung.

only one of the two components of the generally invariable complex: tumor-infection.

(3) We believe that only in the cases with bone invasion (osteolysis in the x-ray film) does the thoracic wall pain syndrome mean that the cancer is inoperable. With this fact in mind we resected 11 cases of cancer of the lung (9.1 per cent) which began with thoracic pain but without osteolysis.

(4) Among the extrathoracic syndromes which occur as onset symptoms we have an important one which is relatively easy to identify and generally pertains to lung cancer susceptible of resection. We are referring to the rheumatoid syndrome. The complete clinical picture of this syndrome comprises clubbing of the fingers and/or the Bamberger-Marie syndrome (rheumatoid pain, swelling of the epiphyses, tumefaction of the joints and thickness of the periosteum as shown by x-ray film). In our series of 120 resected cases this was the second most common onset syndrome, it occurred in 22 (18.3 per cent).

a) This syndrome is almost pathognomonic. A Bamberger-Marie syndrome plus an x-ray shadow casting lesion in the lung means cancer in this organ in 90 per cent of the cases. (See Case 42. Figs. 4-5.)

b) The symptomatology appears relatively early as it precedes the rest of the symptoms (cough, expectoration, pain, etc.).

c) Generally speaking, the Bamberger-Marie syndrome is caused by a small, circumscribed and peripheral cancer of the lung which, in many instances, is an adenocarcinoma of relatively low malignancy with great possibilities of resection. (In a total of 22 cases there were 17 adenocarcinomas, two undifferentiated and three epidermoids.)

(5) Cancer of the lung is consistent with good general appearance on the part of the patient for a long time. This is the reason why general debility as the onset syndrome appeared only in one case (0.8 per cent).

(6) The last onset syndrome in our series was represented by two cases (1.6 per cent) of fever without infection. The fever was persistent and it resisted all medication. We do not know its etiology.

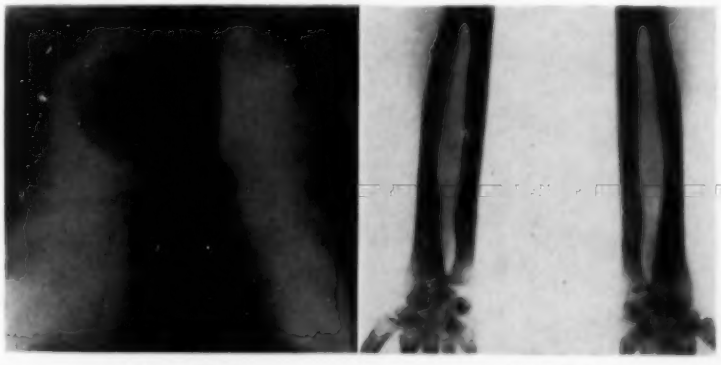

FIGURE 4 FIGURE 5

Figures 4 and 5—(CASE 42): Adenocarcinoma of the lung with Bamberger-Marie Syndrome. Notice the thickness of the periosteum.

Time of Progression:

How long does it take to make a diagnosis of cancer of the lung and to resect it? Logically this depends on two factors:

1) The patient's diligence in going to the doctor's office.

2) The doctor's sagacity in discovering the disease and advising the operation.

These statistics refer to resected cases only, in other words, to cases in which nothing went wrong—the patient consulted the doctor in time, the physician made an exact diagnosis and the cancer itself was not inoperable from the beginning.[3]

In 1.6 per cent of cases cancer was found through a health examination. This is not, of course, the occasion for commenting on the importance of preventive medicine, but we can say that it is in cancer of the lung where we can obtain the best results from yearly health examinations with x-ray films.

A striking onset (i. e. hemoptysis) leads to a quick diagnosis. In 21.6 per cent of cases the diagnosis was made within six months and in 22.5 per cent the etiology was established in a year!

In 11.6 per cent of the cases the diagnosis was made after a year and a half.

As statistics showed us that we could resect a cancer of the lung after the disease had existed for two years (2.5 per cent) and even when it had been present more than two years (3.3 per cent), we can say that only three years after a resection may we begin to think in terms of true survival statistics.

Radiologic Appearance:

The radiologic appearance of removable cancer of the lung is important. The disease always shows itself on the x-ray film. In our statistics we have

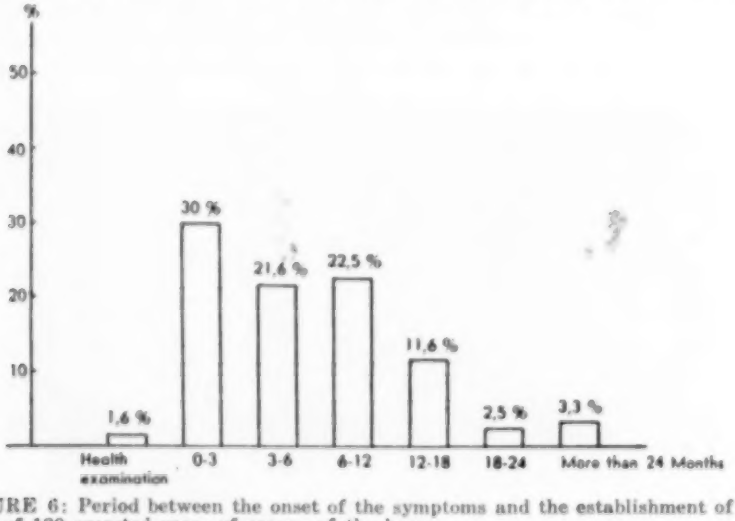

FIGURE 6: Period between the onset of the symptoms and the establishment of diagnosis of 120 resected cases of cancer of the lung.

classified the images into two kinds: those surrounding the hilum and those located peripherally. Those of the first type appear when the disease is localized in the large bronchi (main and lobar). In these cases all the vascular and bronchial elements of the hilum superimpose themselves on the tumor shadow and the result is "unilateral increase of the hilum density," as expressed by Olds and Kirklin.[4]

The hilar localization of a cancer of the lung can produce, depending upon its physiopathogenesis, two different kinds of phenomena with remarkably well defined radiological characteristics:

a) Atelectasis.

b) Emphysema (obstructive or vicarious).

All authors agree that unquestionably the hilar localization of cancer of the lung is more frequent (65 per cent) than the peripheral. These statistical data, however, include all sorts of cancer of the lung. On the other hand, the figures change when we speak only about resected cancer. In our 120 cases we had 32.3 per cent hilar and 67.7 per cent peripheral localizations. This shows that the extra-hilar localization is more favorable to the removal of the growth. In other words, the hilum cancer has a bad prognosis of being resected. The removable cancers, either undifferentiated or adenocarcinomas, are generally peripheral (87.3 per cent and 90.1 per cent, respectively). On the other hand, in the epidermoid type the hilar (53.7 per cent) is slightly more common than the peripheral (46.3 per cent) localization.

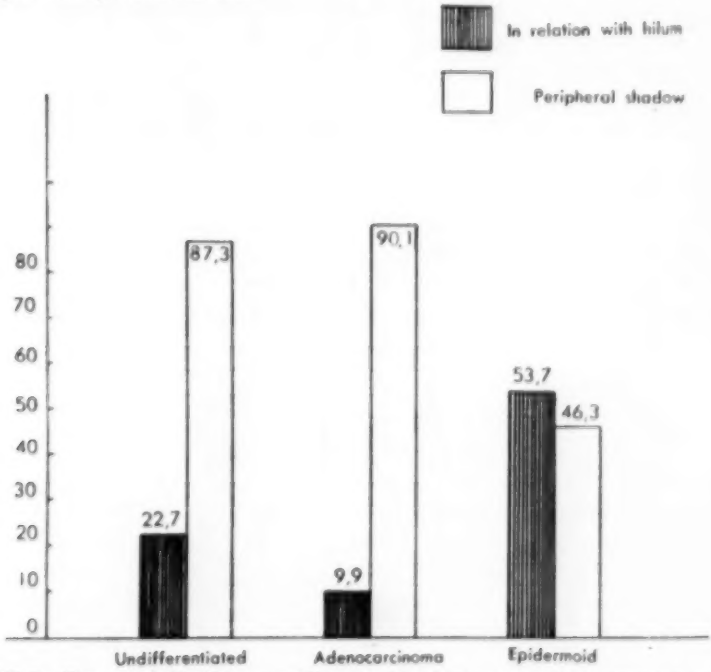

FIGURE 7: X-ray localization according to histologic type (120 resected cases of cancer of the lung).

Bronchoscopy:

In our series of 120 cases, bronchoscopy was performed in 88 with the following results: it was positive (by direct or indirect signs) in 42.3 per cent and negative in 57.7 per cent of the cases. Thus we can say that from the standpoint of resection negative bronchoscopy is favorable. Negative bronchoscopy can by no means rule out a diagnosis of cancer of the lung made on clinical and radiological grounds. When bronchoscopy is positive it confirms the diagnosis.

If we recall the figures of radiological localization (67.7 per cent peripheral and 32.3 per cent hilar) we find that they bear a logical relation to the negative and positive bronchoscopic findings. Undifferentiated cancer with a 22.7 per cent hilar localization showed 35.7 per cent positive bronchoscopies. Adenocarcinoma, almost exclusively located peripherally (90.1 per cent), showed 86.2 per cent negative bronchoscopies. On the other hand, the epidermoid type, located nearest to the hilum in our resected cases (53.7 per cent), showed 62.2 per cent positive bronchoscopies.

Laboratory:

The laboratory is of great help in the study of bronchoscopic and punch biopsies and in the examination of sputum. In both instances we are searching for neoplastic cells. In our 120 resected cases laboratory procedures allowed us to perform the operation with an accurate histologic diagnosis in only 20 patients (16.6 per cent).

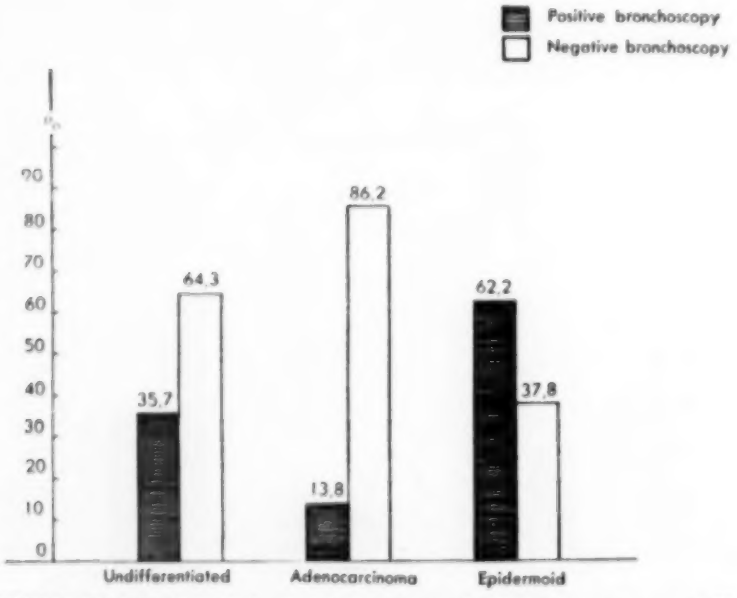

FIGURE 8: Distribution of the positive and negative bronchoscopy among 88 cases.

Differential Diagnosis and Discussion:

We have seen the small or trivial importance of symptoms in the "useful period" of cancer of the lung (we call "useful" the period in which the tumor can be removed). The only exception to trivial symptoms is hemoptoic expectoration. In most cases (100 patients) the diagnosis was based on clinico-radiological criteria.

1) *Tuberculosis.* Of the three types of tuberculosis—infiltrative, tumor-like and cavitary—we can only mistake cancer with the first, because the differentiation from a tuberculous cavity is easy and tumor-like tuberculosis is as susceptible of removal as is cancer itself.

2) *Chronic Suppuration of the Lung.* Although hemoptysis or hemoptoic expectoration and thoracic wall pain could guide us, erroneous diagnoses were frequently made. We must remember that two of the most common onset syndromes of cancer of the lung, bronchial with pneumonitis and bronchial catarrhal (28.3 per cent of the total onset syndromes in our series), have clinical symptomatology similar to that of lung suppuration. The use of antibiotics (1,000,000 units of penicillin and 1 gm. of streptomycin daily for 15 days) was a great help in the differentiation of these diseases. If at the end of 15 days the x-ray shadow remains the same or even grows, we are inclined to consider it cancer.

3) *Hydatid Cyst.* As this is also a surgical disease, its differentiation from cancer is less important.

4) *Fungous Infection of the Lung.* The laboratory helps a great deal in making a correct diagnosis. In many cases, however, in spite of the laboratory, bronchoscopic and radiologic findings, we could not always arrive at a true diagnosis before deciding upon the operation. If so, why then did we send these patients to surgery? We did so because we now have a policy of the "surgical lung," which means that "any chronic lung disease, either inflammatory or not, which acquires tumor-like appearance must be operated," and according to this policy we sent the patients to the surgeon. In this terrible fight against death and time we prefer to operate in time, even if unnecessarily, than to arrive at an exact diagnosis after a long wait.

> "It is better to make a mistake by operating
> than confirm the diagnosis and lose time waiting."

In these cases we could only arrive at a diagnosis of "surgical tumor-like lesion" in which an operation was indicated. The exact diagnosis was made by the pathologist with the frozen section or the organ itself in his hands or by the surgeon during the operation. The criterion to be followed in either case is different. If it is cancer we must wait at least three years to talk about survival. If it is not cancer but one of the other conditions which can be confused with it (hydatid cyst, tuberculoma, syphiloma, chronic abscess, etc.) the prognosis is optimal.

CONCLUSIONS

1) Clinically, resectable cancer of the lung appears as a trivial respiratory condition without any important characteristic of malignancy.

2) In 120 resected cases only one was a woman (0.83 per cent).

3) Physiopathology of cancer of the lung produces three mechanisms:
   a) Bronchial obstruction.
   b) Ulceration and infection.
   c) Extrathoracic manifestations (endocrine?).

4) Fifty-one and six-tenths per cent of the cases began with bronchial symptomatology (cough, catarrh, hemoptysis).

5) The most common onset syndrome was the hemoptoic (28.3 per cent) and the second in order of frequency was the rheumatoid (18.3 per cent).

6) From the point of view of resectability rheumatoid onset syndrome is extremely useful because:
   a) It is almost pathognomonic.
   b) It occurs early.
   c) It appears in small, peripheral tumors which are generally adenocarcinomas of relatively low malignancy.

7) Thoracic pain is not always an index of inoperability except when bone invasion is demonstrated by x-ray film.

8) Bronchoscopy was performed in 88 cases. It was positive in 42.3 per cent and negative in 57.7 per cent. Negative bronchoscopy is favorable to resection because it generally means that the neoplasm is peripheral.

9) In 16.6 per cent of cases the operation was performed after obtaining a true histological proof, and in 83.4 per cent the diagnosis was based on clinical and radiological criteria.

10) Antibiotics were of great importance in differentiating cancer of the lung from chronic suppuration.

11) The doubtful cases, or those in which it was impossible to arrive at an exact diagnosis, were operated according to the criterion of "surgical lung": "any chronic lung disease, either inflammatory or not, which acquires a tumor-like appearance."

RESUMEN

1. Clínicamente, el cáncer del pulmón susceptible de resecarse aparece como una afección respiratoria sin importancia y sin características definidas de malignidad.

2. En 120 casos de resección solo una fué mujer (0.83 por ciento).

3. La fisiopatología del cáncer del pulmón produce tres mecanismos:
   a) Obstrucción bronquial.
   b) Ulceración e infección.
   c) Manifestaciones extratorácicas (endocrinas?).

4. 51.6 por ciento de los casos empezaron con sintomatología-bronquial (tos, catarro, hemoptisis).

5. El modo de principio más común fué el hemoptoico (28.3 por ciento) y el segundo en orden de frecuencia fué el reumatoide (18.3 por ciento).

6. Desde el punto de vista de las posibilidades de resección—el principio de forma reumatoide es de gran utilidad porque:

a) es casi patognomónico.
b) acaece tempranamente y.
c) aparece en tumores periféricos pequeños que generalmente son adenocarcinomas de relativa baja malignidad.

7. El dolor torácico no es siempre un indicio de inoperabilidad excepto cuando se quede demostrar a los rayos X que hay invasión ósea.

8. Se hizo broncoscopia en 88 casos. Fué positiva en 42.3 por ciento y negativa en 57.7. La broncoscopía negativa es favorable para la resección porque generalmente significa que el neoplasma es periférico.

9. En 16.6 por ciento de los casos se realizó la operación después de obtener prueba fehaciente histológica y en 83.4 por ciento el diagnóstico se basó en los criterios clínico y radiológico.

10. Los antibióticos son de gran importancia para diferenciar—el cáncer del pulmón de la supuración crónica.

11. Los casos dudosos, o aquéllos en los que ha sido imposible llegar a un diagnóstico exacto, se operaron de acuerdo con el criterio de "pulmón quirúrgico": "cualquiera enfermedad pulmonar inflamatoria o no que adquiere una apariencia de tumor."

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Chronic Friedlander's Pneumonia

F. ALBERT OLASH, M.D.*
Louisville, Kentucky

Among the bacterial pneumonias, that caused by Klebsiella pneumoniea has always been considered as one of the more serious and most difficult to treat satisfactorily. Soloman[1] estimated that Friedlander's pneumonia constitutes 1 to 3 per cent of all adult cases of pneumonia. The onset of the disease can closely mimic either that of pneumococcic pneumonia or virus pneumonia and failure of the disease to respond to ordinary antibiotics is frequently the first factor to raise a question as to the correct diagnosis. The following case presentations point out the problems in diagnosis and treatment of these conditions and illustrate the difficulties which may arise.

Case 1: E. J. a 57 year old colored male was admitted to the hospital with a chief complaint of shortness of breath. Four days prior to admission he developed a cold, and two days prior to admission he had an acute onset of chills, fever and hemoptysis (bright red blood). The fever, cough and hemoptysis continued until admission, when he appeared acutely ill. The temperature was 101.6° F, pulse 120 and respirations 30 per minute. The blood pressure was 90/50. Examination showed consolidation of the upper lobe of the right lung—and this was confirmed by x-ray film inspection. White blood cell count was 1850 with a differential of 54 neutrophils, 43 lymphocytes, two eosinophils and one monocyte. Urinalysis showed a plus 2 albuminuria and sputum examination revealed Friedlander's bacillus, type B. Supportive therapy was instituted and aqueous penicillin 50,000 units, IM, with streptomycin 0.25 gram, IM, every three hours was given. In spite of this, the patient became more ill, developed frank pulmonary edema and expired within 24 hours. Subsequent reports on blood cultures showed Friedlander's bacilli present. Autopsy showed lobar pneumonia, right upper lobe—due to Friedlander's bacillus, and bilateral necrosis of adrenal cortex, with hemorrhage.

Case 2: M. K. a 64 year old white male was admitted to the hospital with a chief complaint of hemoptysis of two and a half months duration. Six weeks before this admission, he had been treated for pneumonia at another hospital but following discharge his cough and hemoptysis continued and he lost 15 pounds.

His past records showed previous hospitalization four years earlier with pneumococcic pneumonia (Type VII) which was treated with penicillin and which had not completely resolved two months after the acute illness. Bronchoscopy at that time had revealed no malignancy or bronchial obstruction.

On admission his temperature and pulse were normal. The trachea was deviated to the right. Impairment was present over the right upper chest anteriorly and posteriorly, with numerous crackling rales in this area.

Laboratory studies showed white blood cells 11,400 with 72 PMN, 3 PME and 25 lymphocytes. The urinalysis was normal. Sedimentation rate was 32 mm. in one hour. Sputum culture showed Friedlander's bacillus, Type A. Acid fast bacilli were not found.

Chest x-ray film showed a wedge of increased density at the right apex within which there was an area of radiolucency. There was also mediastinal shift to the right.

Bronchoscopy revealed purulent secretions in the right upper lobe bronchus seen only with the right angle scope. No definite tumor mass was visualized. Biopsy was not obtainable but a Papanicolaou specimen was obtained which was reported as Class II.

The presumptive diagnosis was chronic Friedlander's pneumonia but the possibility of superimposed bronchogenic carcinoma could not be excluded. He refused repeat bronchoscopy and was treated with streptomycin and penicillin for 10 days during which time no improvement was noted. When exploratory thoracotomy was done, the right upper lobe felt quite firm suggesting carcinoma. Frozen section pathologic slides

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confirmed this. Pneumonectomy was done. Gross and microscopic examination of the surgical specimen showed unresolved pneumonia with cavitation, fibrosis and chronic inflammation with Friedlander's bacillus type A isolated from the specimen. The bronchi contained a moderate amount of pus but no carcinoma was present in the surgical specimen.

DISCUSSION

Friedlander's pneumonia can be divided into two stages, the acute or primary stage which is frequently a fulminating putrid necrosis of the lung, and the secondary or chronic stage which may occur if the patient survives. Until recent years, there was no adequate treatment for acute Friedlander's pneumonia and the mortality varied from 70 to 80 per cent. When recovery from the acute disease occurred, complications were frequently observed. Within the past eight years the outlook has changed considerably because of the encouraging reports of the effect of streptomycin, chloramphenicol and aureomycin on K. pneumonia. With this more frequent survival of patients, the problems of residual chronic suppurative pneumonia becomes of great importance. (See Chart.)

Whether chronic Friedlander's pneumonia occurs as such from the beginning or as a sequel to acute Friedlander's pneumonia, in either case the final picture after months or years of activity cannot be accurately

ACUTE FRIEDLANDER'S PNEUMONIA

Author	No. of Survivals	Antibiotic	Remarks
Nataro et al[3] (with review of literature)	12	Streptomycin	Two showed x-ray evidence of cavitation or severe fibrosis at the time of discharge or follow-up
Morgan and Hunt[5]	1	Streptomycin	Uneventful recovery
Barber and Grant[1]	4	Streptomycin	Two cases showed residual small cavities with surrounding fibrosis
Kirby and Coleman[2]	1	Chloramphenicol	
	1	Aureomycin—then Streptomycin	All recovered with residual fibrosis and scarring
	1	Penicillin—Streptomycin Sulfadiazine	
	1	Penicillin and Chloramphenicol	Complete recovery
	1	Penicillin, Streptomycin Chloramphenicol	
Drury[6]	1	Aureomycin	Recovery following spontaneous pneumothorax and decortication
Dowling and Lepper[7]	3	Aureomycin	"Prompt recovery"
Wasserman and Pomerantz[4]	1	Chloramphenicol	Uneventful recovery
	1	Chloramphenicol Streptomycin and Sulfadiazine	Residual cavitation requiring lobectomy

predicted. The result may be anything from a fibrosed lobe to an area of mixed bronchiectasis, abscess formation, and fibrosis. In this chronic stage the effect of antibiotic therapy is not so dramatic. The over-all effect is frequently inversely proportional to the degree of chronicity—i. e., the more fibrosis present, the less permanent effect from antibiotics. In this chronic stage, differentiation from fibro-caseous tuberculosis or bronchogenic carcinoma is frequently impossible. The presence of one condition does not exclude the possibility of a combination of diseases. In Hydes[9] series of 51 cases, pulmonary tuberculosis was found as a complication in three individuals, and Belk[10] reporting on 18 cases, showed one to be associated with metastatic carcinoma of the lungs and two with pulmonary tuberculosis. In spite of thorough diagnostic studies including accurate history, x-ray film, bronchoscopy, Papanicolaou examinations and bacteriological studies, one is frequently left without a clear cut diagnosis and in such cases exploratory thoracotomy should be done. Even at operation the differentiation may be difficult and frozen section studies must be utilized.

The presence of chronic suppurative pulmonary disease four to six months after acute Friedlander's pneumonia[11] places the condition in the chronic stage. In this stage treatment with antibiotics should be tried, but past experience in general has shown their effects to be temporary. Combined therapy of antibiotics and pulmonary resection is curative. Resection should be limited to the areas involved and in the majority of cases lobectomy is all that is required.

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Teaching Chest Disease*

The Value of "Gough" Large Lung Sections as Teaching Instruments

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In 1949, Gough and Wentworth, working in the Welsh National School of Medicine, Cardiff, Wales, described a method for the study of the pathologic anatomy of the lung in coal-miner's pneumoconiosis. The method entails the cutting of gelatin embedded, frozen sections of an entire lung by means of a large sliding microtome, and mounting them unstained on filter paper.

In brief outline, the technique is as follows:

The lung is filled through the bronchus with "fixative" until it is fully distended. The bronchus is ligated tightly to prevent the escape of the fixative, and the lung is placed in a large crock containing the same fixative, and allowed to "fix" for a week or longer. Then a large slice, 1" thick, is removed. The slice is taken through a plane selected to show the changes to best advantage. Some pathologists prefer a coronal slice corresponding to the standard antero-posterior x-ray film of the chest. The slice of lung is impregnated with gelatin and "cast" in a block of gelatin and frozen. Frozen sections are cut on a large sliding microtome at 400 microns thickness; floated in water, and then transferred to sheets of "Plexiglas," and eventually covered by three large sheets of filter paper saturated with liquefied gelatin and allowed to dry. On stripping the dried filter paper from the Plexiglas it will be found that the sections have become adherent to and apparently incorporated into the filter paper. An attractive preparation is obtained by spraying the "mounts" front and back with "plastic" aerosol. This thin coating of "plastic" waterproofs the sections and prevents accumulation of dirt and fingerprints. Details of this technique may be found in J. Royal Microscopic Soc., 69:231, 1949; J. Fac. Radio., 1:28, 1949, or from the McIntyre Research Foundation, 25 King Street, W., Toronto, Canada.

These preparations are aesthetically acceptable and actually resemble photographs of the cut surface of the lung (Fig. 1). They may be viewed by either reflected or transmitted light. The sections can be an extremely useful aid in the postmortem study of chest disease. They form a link between gross anatomy and microscopic histology, and will demonstrate the coarser details of the lesions, their extent and location, and the secondary changes that may complicate them. The detail may be studied to advantage by means of a hand magnifying lens. They may be of great help to the radiologist or chest physician in the interpretation of x-ray

*The seventh in a new series of articles prepared under the sponsorship of the Council of Undergraduate Education of the American College of Chest Physicians.
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films of the chest when taken in conjunction with the histologic findings. In this regard, it should be pointed out that the sections are quite translucent, and so may be mounted alongside the x-ray films, in a viewing box and the x-ray shadows compared with the pathologic areas in the lung. In this connection, their use in clinico-pathologic conferences will be obvious. The sections are aesthetically acceptable and because of their resemblance to photographs, it should be possible to use them as adjuncts in bedside teaching where the conventional mounted specimens in glass containers could not be employed.

FIGURE 1: Photograph of large lung section demonstrating the presence of silicotic nodulation and also a large squamous cell carcinoma of the upper lobe. The finished sections approximate the actual lung size and the natural colors are preserved.

ANNUAL MEETINGS

Board of Regents and Board of Governors

The Board of Regents and the Board of Governors held their annual meetings at the Ambassador Hotel, Atlantic City, on Thursday, June 2, in connection with the 21st Annual Meeting of the American College of Chest Physicians. The following Regents, Governors, council and committee members, chapter officials and guests attended these meetings:

Donald R. McKay, Buffalo, New York, Chairman, Board of Regents

David H. Waterman, Knoxville, Tennessee, Chairman, Board of Governors

Osler A. Abbott, Atlanta, Georgia
Donato G. Alarcon, Mexico City, Mexico
Arnold Anderson, St. Petersburg, Florida
Robert J. Anderson, Washington, D. C.
Albert H. Andrews, Chicago, Illinois
Carl C. Aven, Atlanta, Georgia
Charles P. Bailey, Philadelphia, Pennsylvania
Andrew L. Banyai, Milwaukee, Wisconsin
Alvan L. Barach, New York, New York
Gerald Beatty, Wilmington, Delaware
B. Guy Begin, Montreal, Quebec, Canada
Otto L. Bettag, Chicago, Illinois
Antonio Blasi, Naples, Italy
Houck E. Bolton, Philadelphia, Pennsylvania
Francis D. T. Bowen, Hartford, Connecticut
Charles A. Brasher, Mount Vernon, Missouri
Otto C. Brantigan, Baltimore, Maryland
Paul J. Breslich, Minot, North Dakota
John F. Briggs, St. Paul, Minnesota
Alfred A. Busse, Jefferson, Wisconsin
William P. Chester, Detroit, Michigan
Ross K. Childerhose, Harrisburg, Pennsylvania
Dean B. Cole, Richmond, Virginia
Edgar Davis, Washington, D. C.
Leonard C. Evander, Lockport, New York
Seymour M. Farber, San Francisco, California
Max Fleishman, Omaha, Nebraska
M. Jay Flipse, Miami, Florida
Carl H. Gellenthien, Valmora, New Mexico
Frederick L. Giles, Honolulu, Hawaii
Alfred Goldman, Los Angeles, California
Burgess L. Gordon, Philadelphia, Pennsylvania
Edward A. Greco, Portland, Maine
Alvis E. Greer, Houston, Texas
C. Lydon Harrell, Richmond, Virginia
J. E. J. Harris, Albuquerque, New Mexico
W. Elliott Harrison, Vancouver B. C., Canada
John S. Harter, Louisville, Kentucky
Juan R. Herradora, Jersey City, New Jersey
David W. Heusinkveld, Cincinnati, Ohio
Paul H. Holinger, Chicago, Illinois
Willard B. Howes, Detroit, Michigan
William A. Hudson, Detroit, Michigan
Chevalier L. Jackson, Philadelphia, Pennsylvania
Hollis E. Johnson, Nashville, Tennessee
R. E. Joseph, Salem, Oregon
Francis J. Kasheta, Glencliff, New Hampshire
Harold I. Kinsey, Toronto, Ontario, Canada
Francis G. Kravec, Youngstown, Ohio
Alexander Libow, Miami Beach, Florida
Joseph H. Little, Mobile, Alabama

Shelley U. Marietta, Washington, D. C.
George R. Maxwell, Morgantown, West Virginia
Edgar Mayer, New York, New York
Francisco Menendez, Havana, Cuba
Frank A. Merlino, Providence, Rhode Island
Herman J. Moersch, Rochester, Minnesota
Leopoldo Molinari, Lima, Peru
Vincenzo Monaldi, Naples, Italy
Robert B. Morrison, Austin, Texas
Foster Murray, Brooklyn, New York
Jay Arthur Myers, Minneapolis, Minnesota
Antonio Navarrete, Havana, Cuba
James M. Odell, The Dalles, Oregon
Arthur M. Olsen, Rochester, Minnesota
Richard H. Overholt, Boston, Massachusetts
Jerome V. Pace, Rockville, Indiana
J. Winthrop Peabody Sr., Washington, D. C.
Charles K. Petter, Waukegan, Illinois
Joseph C. Placak, Sr., Abingdon, Virginia
Jaime F. Pou, Hato Rey, Puerto Rico
Coleman B. Rabin, New York, New York
Howell Randolph, Phoenix, Arizona
Alfred A. Richman, New York, New York
Antonio Rodriguez Diaz, Havana, Cuba
John Ryder, Calgary, Alberta, Canada
Robert E. Schwartz, Hattiesburg, Mississippi
J. Gordon Seastrunk, Columbia, South Carolina
A. J. Steiner, St. Louis, Missouri
Clifford F. Storey, Portsmouth, Virginia
Lawrence H. Strug, New Orleans, Louisiana
James H. Stygall, Indianapolis, Indiana
Sir Geoffrey Todd, Sussex, England
Richard R. Trail, London, England
Harold G. Trimble, Oakland, California
Darrell H. Trumpe, Springfield, Illinois
Buford H. Wardrip, San Jose, California
Roy A. Wolford, Washington, D. C.
Irving Willner, Newark, New Jersey
W. Bernard Yegge, Denver, Colorado
Murray Kornfeld, Chicago, Illinois, Executive Director
Harriet L. Kruse, Chicago, Illinois, Executive Assistant

The annual Joint Meeting of the Board of Governors and Board of Regents was held at 9:00 a.m. on Thursday, June 2. Dr. David H. Waterman, Chairman of the Board of Governors presided. The Board of Regents met on Thursday afternoon at 2:00 p.m. and again on Sunday, June 5. The Regent of the College for New Jersey, Dr. Irving Willner, who served as Chairman of the Committee on General Arrangements for the 21st Annual Meeting, was introduced and spoke briefly regarding arrangements for the meeting.

The following reports were presented:

REPORT OF THE COMMITTEE ON MEMBERSHIP

Since the last Annual Meeting, 471 new members have been admitted into the College and 78 Associate Fellows were advanced to Fellowship. The present membership of the College is 5204 and our members reside in 86 countries or territories.

In addition to the above members, as of May 10, 1955, we had a total of 50 applications, filed between March 15, 1955 and May 10, 1955, pending approval of the Board of Regents. Of this total, 24 are for Fellowship, 12 for Associate Fellowship, 10 for Associate Membership and 4 for advancement to Fellowship. These applications will be reviewed by the Board of Regents at the Semi-annual Meeting of the College, to be held in Boston, Massachusetts, November 26-28, 1955.

Chevalier L. Jackson, *Chairman*

REPORT OF THE TREASURER

STATEMENT OF INCOME AND EXPENSES FOR THE YEAR ENDED DECEMBER 31, 1954

INCOME:		
Annual Dues		$ 79,637.90
Fellowship Fees		24,125.00
Sales		
Advertising	$35,234.70	
Subscriptions	23,306.17	
Exhibits	1,101.08	
Directory—Net	3,390.81	
College Services—Net	7,250.91	
	$70,283.67	
Less—Discount Allowed	7,197.24	63,086.43
Interest Received on U. S. Savings Bonds		832.50
Interest on Investment in Savings & Loan Assn.		320.83
TOTAL INCOME		$168,002.66
EXPENSES:		
Salaries	$43,856.33	
Printing Journal	48,205.80	
Annual Meeting	8,808.68	
International Meeting	4,136.51	
Building Account (Schedule 1)	3,619.24	
Printing and Engraving	3,233.42	
Handling and Posting Journal	4,795.90	
Postage and Shipping	3,575.55	
Officers' and Committee	3,867.11	
Telephone and Telegraph	2,882.71	
Office Expense	2,013.83	
Traveling—Executive Director	1,977.85	
Semi-Annual Meeting—Board of Regents	1,534.95	
Public Relations	1,631.22	
Editor of Journal	1,800.00	
Hospital Counselor	858.37	
Library	161.59	
Membership Certificates	247.84	
Payroll Taxes	645.61	
Employment Agency Fees	548.00	
President's Secretarial Expense	150.00	
Prize Essay Award	500.00	
Audit	250.00	
Contribution to World Medical Assn.	500.00	
College Medal	90.60	
Contribution to National Society for Medical Research	25.00	
Depreciation—Furniture and Fixtures	1,768.60	
Total Expenses		141,684.71
NET INCOME		$ 26,317.95

Ralph H. Marcus, Certified Public Accountant, Chicago, Illinois.

Charles K. Petter, *Treasurer*

REPORT OF THE PRESIDENT

Dr. Waterman, members of the Boards of Regents and Governors, it is with a mixture of pride and pleasure that I welcome you to this 21st Annual Meeting of the American College of Chest Physicians. This is the time when we of the College should take stock of our inheritance and of the duties and obligations which devolve upon us as we attain our maturity. We should also evaluate in our minds our abilities and our capacity to protect and improve our inheritance and to fulfill our obligations.

We come to our maturity with an inheritance of an international organization with a fellowship of more than 5,000 members in 86 countries, provinces and territories, dedicated to the purpose of study and promotion of knowledge of diseases of the chest among physicians. It is well to remind you that our College has never limited its interest to tuberculosis or any other single disease such as cardiovascular disease or cancer of the lung. Its fellowship is interested in the study and propagation of all knowledge and information concerning all aspects of diseases of the chest. It is because our membership includes these specialists in the broad aspects of diseases of the chest that we are able to bring about an interchange of information dealing with all aspects of diseases of the chest. Pulmonary and cardiovascular problems as we all know, are so closely inter-related that it is necessary to keep informed of the advances being made in each field. I am very pleased that during my term as President, many of the leading cardiologists throughout the country have come into the College. They have found that, through our programs, postgraduate courses and our journal, they can contribute toward the accomplishment of our broad purpose of service to humanity through the physician.

William A. Hudson

REPORT OF THE COUNCIL ON POSTGRADUATE MEDICAL EDUCATION

Postgraduate Courses Sponsored by the Council During the Period, 1946-1955

REGISTRATION

Chicago Courses

1946	25
1947	62
1948	44
1949	38
1950	51
1951	51
1952	65
1953	92
1954	40
1955	Oct. 3-7

New York City Courses

1948	76
1949	86
1950	110
1951	138
1952	97
1953	140
1954	98
1955	Nov. 14-18

Philadelphia Courses

1948	62
1949	44
1950	47
1951	54
1952	87
1953	68
1954	80
1955	93

Milwaukee Courses

1951	68
1952	41
1953	59

San Francisco Courses

1948	43
1949	71
1951	36
1952	43
1954	47

Newark Courses

1951	85
1955	75

Nashville Course

1951	50

New Orleans Course

1954	58

Pittsburgh Courses

1953	40
1955	Oct. 2-9-16-23

TOTAL REGISTRATION, 1946-1955—2,464

A postgraduate course will be presented in Los Angeles, California, December 5-10, 1955. Postgraduate courses on diseases of the chest have been given in the following countries during the period 1951 to the present date: Havana, Cuba—1951-1952 and 1954; Manila, Philippines—1951, 1953 and 1955; Lima, Peru—1953.

The College has cooperated with medical schools and clinics in presenting postgraduate courses in the following cities: Cleveland, Ohio; Denver, Colorado; Houston, Texas; Los Angeles, California; Minneapolis, Minnesota; Portland, Oregon; and Salt Lake City, Utah.

J. Winthrop Peabody, Sr, *Chairman*

Edward Lebovitz, *Vice Chairman*
Alfred S. Dooneief
Chevalier L. Jackson
Hollis E. Johnson
Seymour M. Farber, *Secretary*
Fay A. LeFevre
Edwin R. Levine
Maurice S. Segal

REPORT OF THE COUNCIL ON UNDERGRADUATE MEDICAL EDUCATION

During the year 1953-1954, the Council on Undergraduate Medical Education sponsored the publication of twelve articles on "Modern Concepts in the Teaching of Chest Disease" which appeared in the official journal of the College, DISEASES OF THE CHEST. I am pleased to report that since the fall of 1954, four additional articles on this subject were published in the College journal, and three articles are scheduled for publication in early issues. It is hoped by our Council that these articles will be of assistance to physicians who are engaged in the teaching of medical students.

The Council also sponsored the publication of the book entitled NONTUBERCULOUS DISEASES OF THE CHEST, a companion book to THE COMPLICATIONS OF PULMONARY TUBERCULOSIS, published in 1949, which have received good attention.

This year a committee has been established on Audiovisual Aids, under the chairmanship of Dr. Robert B. Stone of Oakland, California. It is planned that this new committee, in cooperation with the Committee on Motion Pictures, will compile a series of slides and motion pictures which may be used in the teaching of diseases of the chest, and made available to medical schools.

It is my pleasure to report that the New Jersey Chapter of the College sponsored and prepared a film recently on TECHNIQUE OF FLUOROSCOPY OF THE CHEST, directed by Drs. Paul K. Bornstein and Irving J. Selikoff. This film is being reviewed by our Council and the Committee on Motion Pictures for approval in the use of undergraduate medical education. The new film by Drs. Chevalier L. Jackson, John F. Huber and Charles M. Norris, entitled THE BRONCHOPULMONARY SEGMENTS, PART I: ANATOMY AND BRONCHOSCOPY, produced by Pfizer Laboratories, is another excellent motion picture and has been approved by the Committee on Motion Pictures for undergraduate teaching.

The establishment of the annual Essay Contest of the College has been an aid in interesting undergraduate medical students in the field of chest disease. The Committee on College Essay received 25 manuscripts for the 1955 Contest, the highest number submitted since its inception. These essays have been submitted by medical students in the United States, Canada, Australia, England, India, Hong Kong and Scotland.

The Council on Undergraduate Medical Education wishes to acknowledge the splendid cooperation and assistance of the Committees on Motion Pictures, Audiovisual Aids, College Essay and the Editorial Board of DISEASES OF THE CHEST in carrying forward our program.

Edward W. Hayes, Sr. *Chairman*

Theodore H. Noehren, *Vice-Chairman*	Karl H. Pfuetze, *Secretary*
William S. Conklin	Martin J. Sokoloff
Eli H. Rubin	William M. Spear
Robert R. Shaw	Hugh G. Whitehead Jr.

REPORT OF THE COMMITTEE ON MOTION PICTURES

The 1955 program of the annual College meeting shows a change requested by the Motion Picture Committee and approved by the Program Committee. This consists of a continuous film program through the three days running simultaneously with the regular program. Each film is shown at the same time each day to permit anyone a choice of three showings of a film which will avoid a conflict with a part of the program in which he has particular interest. This arrangement has proven most satisfactory at meetings of the AMA and the American College of Surgeons. This trial will be watched with interest by members of the Committee and the College as a whole.

A new list of approved films is being prepared by the Committee, deleting old films and adding new ones. It has been found that, in general, surgical films have the shortest useful life, films depicting physiological or pharmacological problems a somewhat longer useful life, and films on anatomy or pathology the longest useful life. New films are being constantly reviewed for approval by Committee members. Suggestions are forwarded to authors if approval is withheld. It is requested that all members of the College, particularly the key men on the Board of Governors and Regents, inform members of the Committee of new films being prepared in their areas.

At the suggestion of the Committee on Postgraduate and Undergraduate Medical Education the new lists being prepared will designate those films particularly useful for graduate or undergraduate medical education. The list will also serve as a basis for requests for films for Chapter, national and international meetings.

Paul H. Holinger, *Chairman*	H. Corwin Hinshaw
Houck E. Bolton	David H. Waterman
Alfred Goldman	Francis M. Woods

REPORT OF THE COUNCIL ON RESEARCH

It is with considerable pleasure that I report to you the activities of your Council on Research during the past year.

Although many of the objectives that the Council on Research has tried to attain have not been accomplished, there are certain phases that have more than surpassed our expectations. Perhaps it is well to report first on our disappointments. It had been the hope of the Council, as well as the officers of the College, that some method be devised by which a sizable sum of money might be accumulated for the purpose of supporting research by members of the College. In spite of the various plans that have been considered, none so far has met with appreciable success. It is our hope, however, that in the coming years it will be possible to accomplish this aim.

During the past year, the Council on Research has been approached by several drug houses with requests for endorsement or approval of one of their new products. The Council on Research, with the approval of the Board of Regents, set up standards which would have to be met if the College were to undertake the investigation of any product before giving its endorsement. The drug companies were to defray the expenses involved in carrying out such a project, plus a small additional fee for the work of the College in setting up the investigative program. Whatever funds were accumulated by this means would be assigned to the research fund of the Council. The various products that have thus far been submitted to the Council for approval have been known by various members of the College to have been found unsuitable for recommendation, so that no research work of this nature has been carried out up to the present time. Undoubtedly, as time goes on we will have further requests from drug companies for approval of products, especially when it is realized that endorsement by the College would have some significance.

Several members of the College have been granted financial support by the Tobacco Industry Research Committee, and it is to be hoped that these members will give us a report at some future date on the results of their studies. The Council on Research has been willing in all cases to assist any member of the College who has a worth-while research project in making application to the Tobacco Industry Research Committee for financial assistance, and we shall certainly continue to do so in the future.

During the coming year, the College will present its first award for an outstanding thesis pertaining to cardiac disease, to be given by the Committee on Cardiovascular Disease. We do hope that in the years to come there may be further awards for outstanding work in the various fields of cardio-pulmonary disease. We feel this is a practice that is very worth while encouraging.

One of the duties that is delegated to the Council on Research is the co-ordination of the activities of the various scientific committees which are appointed by the College to investigate and develop various problems pertaining to thoracic disease. Definite progress has been made in this plan of co-ordination. One usually associates the development of any research activity or clinical study with the requirement of great sums of money. This is, of course, an active ingredient, but it is refreshing to note that the various committees that constitute the Council on Research have accomplished a great deal by their own unstinted and unselfish generosity. May I briefly refer to a few of the outstanding accomplishments of these various committees, which will be elaborated upon in the individual reports of their chairmen.

The Committee on Chemotherapy and Antibiotics, under the chairmanship of Dr. Pfuetze, has made an exhaustive study of the chemotherapeutic agents that are at present available in the treatment of tuberculosis, and a report of its work has already appeared in DISEASES OF THE CHEST. The Committee on Surgical Treatment is at the present time in the process of preparing a book for publication that should be a distinct asset and a worthy mate to the book already published on the diagnosis of pulmonary disease under the guidance of Dr. Banyai. The program that this Committee has outlined for the future is a most ambitious one, and Dr. Goldman, the Chairman, will report on this to you.

The Committee on Cardiovascular Diseases, under the chairmanship of Dr. Briggs, and its various sub-committees, have been most active during the past year. At the present time the Section on Cardiovascular Surgery, under the direction of Dr. Bailey, is reporting on a study of over a thousand cases of patent ductus arteriosus that have been treated surgically. They are hopeful of making a similar study of other types of cardiac abnormalities. Under Dr. Master's leadership a study of blood pressure in the aged is being pursued with considerable vigor. The Committee on Physiologic Treatment, of which Dr. Andrews is Chairman, has been most active and has developed an exhibit on inhalation therapy that has received favorable comment wherever it has been displayed. This Committee has also been instrumental in guiding the development of the American Association for Inhalation Therapists.

The Committee on Nonsurgical Therapy, under the chairmanship of Dr. Trimble, is continuing with its very interesting case studies which have been so instructive in the past, and will carry out a study on bed rest in tuberculosis in a similar manner. The Committee on Broncho-esophagology, of which Dr. Olsen is Chairman, has been especially interested in studying the problem of adequate training for those engaged in the field of broncho-esophagology. The Committee on Asthma, which is the newest committee to be established, has not as yet had sufficient time to develop a full-fledged program, but is in the process of doing so.

May I at this time take the opportunity to thank the chairmen of the various subcommittees who have been most co-operative in every way and whose personalities and keen minds have been most stimulating to me. I also wish to thank the executive officers of the College who at all times have given us the greatest possible co-operation in any problem that has been presented to us for consideration.

H. J. Moersch, *Chairman*

Alvan L. Barach, *Vice-Chairman*
Albert H. Andrews
John F. Briggs
Alfred Goldman
Harold G. Trimble, *Secretary*
Arthur M. Olsen
Karl H. Pfuetze
Leon Unger

REPORT OF ACTIVITIES OF THE COMMON COLD FOUNDATION

Following the annual meeting of the Foundation held on June 8, 1954 in New York City, emphasis was placed on strengthening the membership of the Medical and Scientific Advisory Committees. On September 21, 1954, a luncheon meeting was held to which were invited the Medical Directors of the larger companies in the New York area. Fifty-five companies were represented at this luncheon. The first appeal for funds was made on November 10, 1954, following a meeting at the Union League Club for industrial leaders in the New York area. On February 11, 1955 the Foundation co-sponsored a Symposium on the Common Cold with the Microbiology and Immunology Study Section of the National Institutes of Health. The members of the Scientific Advisory Committee met on February 12, 1955 to consider applications for grants and to establish procedures for processing. The Common Cold Foundation was invited to have a scientific exhibit at the National Industrial Medical Conference, April 24-29, at Buffalo, New York. This was accepted and the work now being done at the Johns Hopkins University under a grant from the Foundation and from the U. S. Public Health Service was shown. On May 1, 1955, the Scientific Advisory Committee met in Atlantic City to review additional grant applications. Those approved will be activated as rapidly as funds permit. A meeting will be held on June 14 for industry leaders in the New York Area and another appeal for funds will be made at that time. Dr. Thomas Francis, Jr., will be the principal speaker at this meeting. Since the initial appeal for funds, November 10, 1954, forty-seven companies have contributed to the Common Cold Foundation. We appreciate the interest of the American College of Chest Physicians in the activities of the Foundation.

Edgar Mayer, *President*

An article entitled "Participation of Physicians in Private Practice in Basic Tuberculosis Control Procedures" prepared and approved by the Council on Public Health was presented to the Board of Regents by the Chairman, Dr. Robert J. Anderson, and accepted. The article will appear in an early issue of DISEASES OF THE CHEST.

In the absence of Dr. Arthur M. Olsen, Chairman of the Committee on Bronchoesophagology, Dr. Alvan L. Barach, Vice-Chairman of the Council on Research, presented an editorial on "Problems in the Training of Bronchoesophagologists" prepared by the committee and approved by the Council on Research. The Board of Regents approved the publication of the editorial in an early issue of DISEASES OF THE CHEST.

Elections:

Dr. Carl H. Gellenthien, Valmora, New Mexico, was elected to the Committee on Nominations to represent the Board of Regents.

Dr. Seymour M. Farber, San Francisco, California, was re-elected a member of the Executive Council.

Dr. John F. Briggs, St. Paul, Minnesota, was elected Chairman of the Board of Regents to succeed Dr. Donald R. McKay of Buffalo, New York.

Dr. Buford H. Wardrip, San Jose, California, was elected to the Committee on Nominations to represent the Board of Governors.

Dr. David H. Waterman, Knoxville, Tennessee, was re-elected as Chairman of the Board of Governors.

Announcements

The Interim Session of the College will be held at the Sheraton Plaza Hotel, Boston, Massachusetts, November 27 and 28, 1955. Dr. Richard H. Overholt of Boston was appointed Chairman of the Committee on Scientific Program.

Plans are progressing for the Fourth International Congress on Diseases of the Chest to be held in Cologne, Germany, August 19-23, 1956. Professor Gerhard Domagk, the discoverer of the sulphonamides and Nobel Prize Winner, has accepted appointment to serve as the President of the Congress. It was further announced that information relative to the arrangements for the Congress would be mailed to the College membership in the near future.

The Board of Regents expressed its appreciation to the members of the New Jersey committees for their splendid cooperation and efforts in making the 21st Annual Meeting of the College successful. The appreciation of the Board of Regents was also extended to the members of the Ladies Reception Committee for the excellent arrangement of the ladies' functions. The Board expressed their gratitude to Mr. Kornfeld and the College staff members for their fine work. It was voted to express the appreciation of the College to the staff of the Ambassador Hotel for their courtesy and cooperation.

1955 PRIZE ESSAY WINNER

Left to right: Dr. William A. Hudson, Detroit, President; Dr. Foster Murray, Brooklyn, Chairman, College Essay Committee; Dr. Stanley William Olson, Dean, Baylor University, Houston; Dr. Hyman Florence, Houston, Essay winner; photographed at the Annual Presidents' Banquet of the College, Atlantic City, June 4, 1955.

1955 Prize Essay Contest

Announcement of the winners of the 1955 Prize Essay Contest of the College was made at the Annual Presidents' Banquet held at the Ambassador Hotel, Atlantic City, June 4, at the time of the 21st Annual Meeting. The first prize winner, Dr. Hyman Florence of Houston, Texas, who had received his degree of Doctor of Medicine at Baylor University College of Medicine just a few days before, was present at the banquet and was presented the First Prize Certificate and cash award in the amount of $250.00 by Dr. Foster Murray, Brooklyn, New York, Chairman of the Committee on College Essay. Also present was Dr. Stanley William Olson, Dean of Baylor University College of Medicine. The essay submitted by Dr. Florence was titled "Atypical Acid-Fast (Chromogenic) Organisms Complicating Pulmonary Disease."

The other winners of the 1955 Contest were as follows:

Allen H. Kline, Senior Class, Baylor University College of Medicine, Houston, Texas, received Second Prize Certificate and a $100.00 cash award for his essay "Diagnosis and Treatment of the More Common Congenital Heart Diseases."

There was a tie for third place and two third prizes have therefore been awarded. Otto Appenzeller and William Victor Benz, students at the New Medical School, University of Sydney, Australia, received Third Prize Certificate and a $50.00 cash award for their essay "A Rational Approach to the Treatment and Diagnosis of Pulmonary Heart Disease."

E. Arthur Calkins, Third Year Student at the College of Medical Evangelists, Los Angeles, California was also awarded a Third Prize Certificate and a $50.00 cash award for his essay "The Superior Vena Caval Syndrome, Report of 21 Cases."

The second and third prize winners are receiving their awards at appropriate ceremonies arranged in their respective cities.

The 1956 Prize Essay Contest is now open to undergraduate medical students throughout the world. The Board of Regents has recommended that members of the College affiliated with medical schools be urged to bring the contest to the attention of the student body at their respective schools. Essays may be submitted on any phase of cardiac or pulmonary diseases. Three prizes will again be awarded comprising certificates and cash awards in the amounts of $250.00, $100.00 and $50.00. The contest will close on April 10, 1956 and instructions for the preparation of manuscripts are as follows:

1) Five copies of the manuscript typewritten in English (double spaced) should be submitted to the Committee on College Essay, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, U.S.A.
2) The only means of identification of the author shall be a motto or other device on the title page and a sealed envelope bearing the same motto on the outside, enclosing the name and address of the author.
3) A letter from the Dean or Chairman of the Department of Medicine or Surgery of the medical school, certifying that the author is a medical student.

College Chapter News

MICHIGAN CHAPTER

The Michigan Chapter will meet jointly with the state medical society at the hotel Pantland, Grand Rapids on September 28. Dr. C. C. Birkelo, Detroit, will speak on "Solitary Lung Lesions."

PENNSYLVANIA CHAPTER

New officers of the Pennsylvania Chapter, elected on June 3, are:

President:	John V. Foster, Harrisburg
Vice-President:	Peter A. Theodos, Philadelphia
Secretary-Treasurer:	Ruth W. Wilson, Beaver

KENTUCKY CHAPTER

The Kentucky Chapter will meet at the Brown Hotel, Louisville, September 29, in conjunction with the meeting of the state medical association. At the chapter luncheon meeting, Dr. Edgar Medlar, Ithaca, New York, will speak on "The Continuing Problem of Tuberculosis as a Pathologist Sees It." The chapter will present the following program in the afternoon:

"Case Reports with Films"
Robert H. Akers, Louisville

"Present Status of Cardiac Surgery"
John S. Harter, J. Ray Bryant, and W. Buford Davis, Louisville

"The Residue of Disease after Chemotherapy"
Edgar Medlar, Ithaca, New York

CUBAN CHAPTER

The Cuban Chapter held its annual meeting in Havana in February. The following officers were elected:

President:	Orfilio Suarez de Bustamante, Havana
Vice-President:	Armando Nunez Nunez, Havana
Secretary-Treasurer:	Francisco Perez Carballas, Havana

SOUTHERN CHAPTER OF SOUTH AFRICA

The Southern Chapter in South Africa held its 66th meeting on April 4, in connection with the annual meeting of the Chapter. Dr. David P. Marais, Cape Town, Regent of the College for South Africa, was awarded the Bronze Medal of the South African Medical Association for his services to the medical association and to the medical profession in the field of tuberculosis. The presentation will be made at the Annual Congress of the medical association, to be held in Pretoria in October. The chapter elected the following officers:

President:	David P. Marais, Cape Town
Vice-President:	Theodore Schrire, Cape Town
Secretary:	Hendrik Muller, Cape Town
Treasurer:	Michael Bailey, Cape Town

NORTHERN CHAPTER OF SOUTH AFRICA

The Northern Chapter of South Africa held its annual meeting and dinner on May 25. The retiring President, Professor J. K. Bremer of Pretoria spoke on "The Use of Cooling in Cardiac Surgery." The following officers were elected:

President:	Albert Rabinowitz, Johannesburg
Vice-President:	David I. Adler, Johannesburg
Secretary-Treasurer:	Dennis N. Fuller, Johannesburg

TEXAS CHAPTER

New officers of the Texas chapter of the College, elected in Fort Worth on April 24 are:

President:	Samuel Topperman, Tyler
First Vice-President:	Walter C. Brown, Corpus Christi
Second Vice-President:	John A. Wiggins, Fort Worth
Secretary-Treasurer:	J. O. Armstrong, Dallas

ITALIAN CHAPTER

The Italian Chapter held its Third Scientific Session on May 15 at the Carlo Forlanini Institute in Rome. Professor A. Omodei Zorini, Regent of the College for Italy, presided and presented the opening address. Among the guests who attended were Professor P. Valdoni, Director of the Institute of Surgical Pathology of the University of Rome, Professor G. Costantini, President of the Italian Federation Against Tuberculosis, and Professor G. Ferreri, Director of the Oto-Rhino-Laryngologic Clinic of the University of Rome.

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Staff physician wanted for a modern, well-equipped and staffed, 210 bed tuberculosis hospital located in an attractive mid-western city of 180,000. Applicant must be sober, industrious, and qualified for Michigan license. Salary commensurate with qualifications and experience. Please address all inquiries to Box 280A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Director, Division of Tuberculosis Control, wanted for staff of Alaska Department of Health with headquarters in Anchorage, Alaska. Applicant must have had postgraduate training in clinical tuberculosis or public health, and at least four years successful experience in the practice of medicine, of which two years must have been in an administrative position in public health or in clinical tuberculosis practice. Salary approximately $15,000 per annum. Apply Alaska Department of Health, Alaska Office Building, Juneau, Alaska.

Resident physician wanted. Tuberculosis experience essential. Call or write Deborah Sanatorium, Browns Mills, New Jersey.

CALENDAR OF EVENTS

NATIONAL AND INTERNATIONAL MEETINGS

Interim Session, American College of Chest Physicians
Sheraton-Plaza Hotel, Boston, November 27-28, 1955

Fourth International Congress on Diseases of the Chest
Council on International Affairs
American College of Chest Physicians
Cologne, Germany, August 19-23, 1956

POSTGRADUATE COURSES

10th Annual Postgraduate Course on Diseases of the Chest
Hotel Knickerbocker, Chicago, Illinois, October 3-7, 1955

2nd Postgraduate Course on Diseases of the Chest
Hotel Roosevelt, Pittsburgh, Pennsylvania, October 2, 9, 16, 23, 1955
(four consecutive Sundays)

8th Annual Postgraduate Course on Diseases of the Chest
Park-Sheraton Hotel, New York City, November 14-18, 1955

Postgraduate Course on Diseases of the Chest
Ambassador Hotel, Los Angeles, California, December 5-10, 1955

CHAPTER MEETINGS

Pennsylvania Chapter, Pittsburgh, September 21, 1955
Rocky Mountain Chapter, Denver, Colorado, September 24, 1955
Michigan Chapter, Grand Rapids, September 28, 1955
Kentucky Chapter, Louisville, September 29, 1955
Potomac Chapter, White Sulphur Springs, Virginia, October 7, 1955
Virginia Chapter, Richmond, October 16, 1955
North Carolina Chapter, Oteen, October 17, 1955
Indiana Chapter, French Lick, October 18, 1955
Southern Chapter, Houston, Texas, November 13-14, 1955

ANNOUNCING . . .

FALL POSTGRADUATE COURSES ON DISEASES OF THE CHEST

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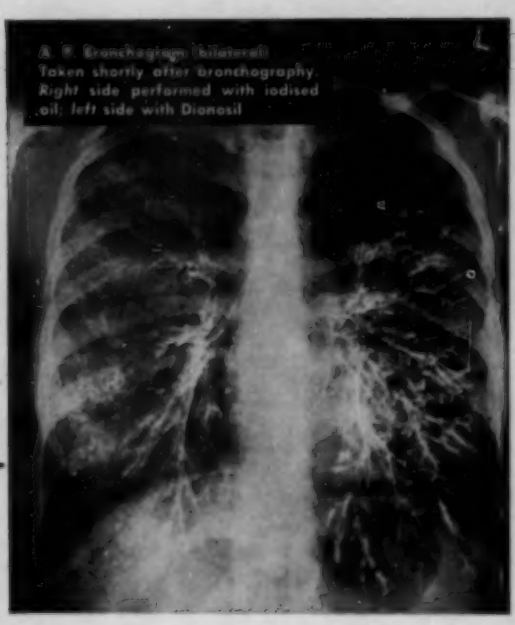
Glenroy N. Pierce, M.D., San Francisco
Donald F. Rowles, M.D., Oakland
James Kieran, M.D., Oakland
Robert Stone, M.D., Oakland
William B. Leftwich, M.D., Oakland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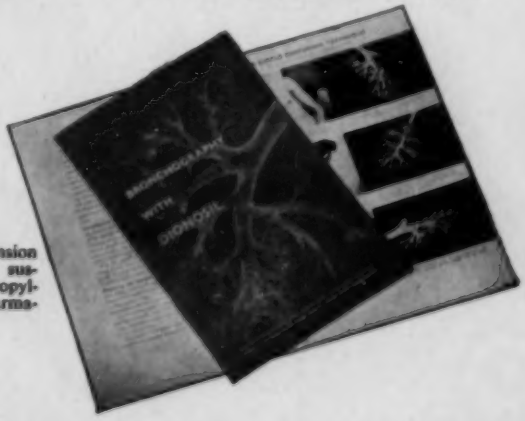

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